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(54) Title: SYNTHETIC PEPTIDES AND USES THEREFORE

(57) Abstract: A synthetic polypeptide is disclosed, which comprises a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide. Synthetic polynucleotides are also disclosed that code for the synthetic polypeptides of the invention as well as expression constructs comprising the synthetic polynucleotides. Also disclosed are methods for constructing the aforementioned molecules and immunopotentiating compositions and methods for treating and/or preventing a disease or condition.

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SYNTHETIC PEPTIDES AND USES THEREFORE

FIELD OF THE INVENTION

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THIS INVENTION relates generally to agents for modulating immune responses. More particularly, the present invention relates to a synthetic polypeptide comprising a plurality of different segments of a parent polypeptide, wherein the segments are linked to each other such that one or more functions of the parent polypeptide are impeded, abrogated or otherwise altered and such that the synthetic polypeptide, when introduced into a suitable host, can elicit an immune response against the parent polypeptide. The invention also relates to synthetic polynucleotides encoding the synthetic polypeptides and to synthetic constructs comprising these polynucleotides. The invention further relates to the use of the polypeptides and polynucleotides of the invention in compositions for modulating immune responses. The invention also extends to methods of using such compositions for prophylactic and/or therapeutic purposes.

Bibliographic details of various publications referred to in this specification are collected at the end of the description.

BACKGROUND OF THE INVENTION

The modern reductionist approach to vaccine and therapy development has been pursued for a number of decades and attempts to focus only on those parts of pathogens or of cancer proteins which are relevant to the immune system. To date the performance of this approach has been relatively poor considering the vigorous research carried out and the number of effective vaccines and therapies that it has produced. This approach is still being actively pursued, however, despite its poor performance because vaccines developed using this approach are often extremely safe and because only by completely understanding the immune system can new vaccine strategies be developed.

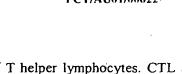
One area that has benefited greatly from research efforts is knowledge about how the adaptive immune system operates and more specifically how T and B cells learn to recognise specific parts of pathogens and cancers. T cells are mainly involved in cell-mediated immunity whereas B cells are involved in the generation of antibody-mediated immunity. The two most important types of T cells involved in adaptive cellular immunity

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are αβ CD8⁺ cytotoxic T lymphocytes (CTL) and CD4⁺ T helper lymphocytes. CTL are important mediators of cellular immunity against many viruses, tumours, some bacteria and some parasites because they are able to kill infected cells directly and secrete various factors which can have powerful effects on the spread of infectious organisms. CTLs recognise epitopes derived from foreign intracellular proteins, which are 8-10 amino acids long and which are presented by class I major histocompatibility complex (MHC) molecules (in humans called human lymphocyte antigens - HLAs) (Jardetzky et al., 1991; Fremont et al., 1992; Rotzschke et al., 1990). T helper cells enhance and regulate CTL responses and are necessary for the establishment of long-lived memory CTL. They also inhibit infectious organisms by secreting cytokines such as IFN-γ. T helper cells recognise epitopes derived mostly from extracellular proteins which are 12-25 amino acids long and which are presented by class II MHC molecules (Chicz et al., 1993; Newcomb et al., 1993). B cells, or more specifically the antibodies they secrete, are important mediators in the control and clearance of mostly extracellular organisms. Antibodies recognise mainly conformational determinants on the surface of organisms, for example, although sometimes they may recognise short linear determinants.

Despite significant advances towards understanding how T and linear B cell epitopes are processed and presented to the immune system, the full potential of epitopebased vaccines has not been fully exploited. The main reason for this is the large number of different T cell epitopes, which have to be included into such vaccines to cover the extreme HLA polymorphism in the human population. The human HLA diversity is one of the main reasons why whole pathogen vaccines frequently provide better population coverage than subunit or peptide-based vaccine strategies. There is a range of epitopebased strategies though which have tried to solve this problem, e.g., peptide blends, peptide conjugates and polyepitope vaccines (ie comprising strings of multiple epitopes) (Dyall et al., 1995; Thomson et al., 1996; Thomson et al., 1998; Thomson et al., 1998). These approaches however will always be sub optimal not only because of the slow pace of epitope characterisation but also, because it is virtually impossible for them to cover every existing HLA polymorphism in the population. A number of strategies have sought to avoid both problems by not identifying epitopes and instead incorporating larger amounts of sequence information e.g., approaches using whole genes or proteins and approaches that mix multiple protein or gene sequences together. The proteins used by these strategies

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however sometimes still function and therefore can compromise vaccine safety e.g., whole cancer proteins. Alternative strategies have tried to improve the safety of vaccines by fragmenting the genes and expressing them either separately or as complex mixtures e.g., library DNA immunisation or by ligating such fragments back together. These approaches are still sub-optimal because they are too complex, generate poor levels of immunity, cannot guarantee that all proteins no longer function and/or that all fragments are present, which compromises substantially complete immunological coverage.

The lack of a safe and efficient vaccine strategy that can provide substantially complete immunological coverage is an important problem, especially when trying to develop vaccines against rapidly mutating and persistent viruses such as HIV and hepatitis C virus, because partial population coverage could allow vaccine-resistant pathogens to reemerge in the future. Human immunodeficiency virus (HIV) is an RNA lentivirus virus approximately 9 kb in length, which infects CD4+T cells, causing T cell decline and AIDS typically 3-8 years after infection. It is currently the most serious human viral infection, evidenced by the number of people currently infected with HIV or who have died from AIDS, estimated by the World Health Organisation (WHO) and UNAIDS in their AIDS epidemic update (December 1999) to be 33.6 and 16.3 million people, respectively. The spread of HIV is also now increasing fastest in areas of the world where over half of the human population reside, hence an effective vaccine is desperately needed to curb the spread of this epidemic. Despite the urgency, an effective vaccine for HIV is still some way off because of delays in defining the correlates of immune protection, lack of a suitable animal model, existence of up to 8 different subtypes of HIV and a high HIV mutation rate.

A significant amount of research has been carried out to try and develop a vaccine capable of generating neutralising antibody responses that can protect against field isolates of HIV. Despite these efforts, it is now clear that the variability, instability and inaccessibility of critical determinants on the HIV envelope protein will make it extremely difficult and perhaps impossible to develop such a vaccine (Kwong et al., 1998). The limited ability of antibodies to block HIV infection is also supported by the observation that development of AIDS correlates primarily with a reduction in CTL responsiveness to HIV and not to altered antibody levels (Ogg et al., 1998). Hence CTL-mediated and not antibody-mediated responses appear to be critical for maintaining the asymptomatic state

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in vivo. There is also some evidence to suggest that pre-existing HIV-specific CTL responses can block the establishment of a latent HIV infection. This evidence comes from a number of cases where individuals have generated HIV-specific CTL responses without becoming infected and appear to be protected from establishing latent HIV infections despite repeated virus exposure (Rowland-Jones et al., 1995; Parmiani 1998). Taken together, these observations suggest that a vaccine capable of generating a broad range of strong CTL responses may be able to stop individuals from becoming latently infected with HIV or at least allow infected individuals to remain asymptomatic for life. Virtually all of the candidate HIV vaccines developed to date have been derived from subtype B HIV proteins (western world subtype) whereas the majority of the HIV infections worldwide are caused by subtypes A/E or C (E and A are similar except in the envelop protein)(referred to as developing world subtypes). Hence existing candidate vaccines may not be suitable for the more common HIV subtypes. Recently, there has been some evidence that B subtype vaccines may be partially effective against other common HIV subtypes (Rowland-Jones et al., 1998). Accordingly, the desirability of a vaccine still remains, whose effectiveness is substantially complete against all isolates of all strains of HIV.

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SUMMARY OF THE INVENTION

The present invention is predicated in part on a novel strategy for enhancing the efficacy of an immunopotentiating composition. This strategy involves utilising the sequence information of a parent polypeptide to produce a synthetic polypeptide that comprises a plurality of different segments of the parent polypeptide, which are linked sequentially together in a different arrangement relative to that of the parent polypeptide. As a result of this change in relationship, the sequence of the linked segments in the synthetic polypeptide is different to a sequence contained within the parent polypeptide. As more fully described hereinafter, the present strategy is used advantageously to cause significant disruption to the structure and/or function of the parent polypeptide while minimising the destruction of potentially useful epitopes encoded by the parent polypeptide.

Thus, in one aspect of the present invention, there is provided a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

In one embodiment, the synthetic polypeptide consists essentially of different segments of a single parent polypeptide.

In an alternate embodiment, the synthetic polypeptide consists essentially of different segments of a plurality of different parent polypeptides.

Suitably, said segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to that of corresponding segments in said at least one parent polypeptide.

Preferably, at least one of said segments comprises partial sequence identity or homology to one or more other said segments. The sequence identity or homology is preferably contained at one or both ends of said at least one segment.

In another aspect, the invention resides in a synthetic polynucleotide encoding the synthetic polypeptide as broadly described above.

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According to yet another aspect, the invention contemplates a synthetic construct comprising a said polynucleotide as broadly described above that is operably linked to a regulatory polynucleotide.

In a further aspect of the invention, there is provided a method for producing a synthetic polynucleotide as broadly described above, comprising:

- linking together in the same reading frame a plurality of nucleic acid sequences encoding different segments of at least one parent polypeptide to form a synthetic polynucleotide whose sequence encodes said segments linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

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Preferably, the method further comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking said fragments together in a different relationship relative to their linkage in said parent polypeptide sequence. In a preferred embodiment of this type, the fragments are randomly linked together.

Suitably, the method further comprises reverse translating the sequence of a respective parent polypeptide or a segment thereof to provide a nucleic acid sequence encoding said parent polypeptide or said segment. In a preferred embodiment of this type, an amino acid of said parent polypeptide sequence is reverse translated to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest. Suitably, an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence (e.g., a palindromic sequence or a duplicated sequence) that is refractory to the execution of a task (e.g., cloning or sequencing).

In another aspect, the invention encompasses a computer program product for designing the sequence of a synthetic polypeptide as broadly described above, comprising:

- code that receives as input the sequence of at least one parent polypeptide;
- code that fragments the sequence of a respective parent polypeptide into fragments;

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- code that links together said fragments in a different relationship relative to their linkage in said parent polypeptide sequence; and
 - a computer readable medium that stores the codes.

In yet another aspect, the invention provides a computer program product for designing the sequence of a synthetic polynucleotide as broadly described above, comprising:

- code that receives as input the sequence of at least one parent polypeptide;
- code that fragments the sequence of a respective parent polypeptide into fragments;
- code that reverse translates the sequence of a respective fragment to provide a
 nucleic acid sequence encoding said fragment;
 - code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence; and
 - a computer readable medium that stores the codes.

In still yet another aspect, the invention provides a computer for designing the sequence of a synthetic polypeptide as broadly described above, wherein said computer comprises:

- (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
 - (b) a working memory for storing instructions for processing said machine-readable data;
- (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polypeptide sequence; and
 - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence.

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In a preferred embodiment, the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking together said fragments in a different relationship relative to their linkage in the sequence of said parent polypeptide.

In still yet another aspect, the invention resides in a computer for designing the sequence of a synthetic polynucleotide as broadly described above, wherein said computer comprises:

- (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
- (b) a working memory for storing instructions for processing said machine-readable data;
- (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polynucleotide sequence; and
- (d) an output hardware coupled to said central processing unit, for receiving said synthetic polynucleotide sequence.

In a preferred embodiment, the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments, reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment and linking together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence.

According to another aspect, the invention contemplates a composition, comprising an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, together with a pharmaceutically acceptable carrier.

The composition may optionally comprise an adjuvant.

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In a further aspect, the invention encompasses a method for modulating an immune response, which response is preferably directed against a pathogen or a cancer, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, or a composition as broadly described above.

According to still a further aspect of the invention, there is provided a method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polypucleotide as broadly described above and a synthetic construct as broadly described above, or a composition as broadly described above.

The invention also encompasses the use of the synthetic polypeptide, the synthetic polynucleotide and the synthetic construct as broadly described above in the study, and modulation of immune responses.

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BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a diagrammatic representation showing the number of people living with AIDS in 1998 in various parts of the world and most prevalent HIV clades in these regions. Estimates generated by UNAIDS.

Figure 2 is a graphical representation showing trends in the incidence of the common HIV clades and estimates for the future. Graph from the International Aids Vaccine Initiative (IAVI).

Figure 3 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV gag [SEQ ID NO: 1] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV gag protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 4 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV pol [SEQ ID NO: 2] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV pol protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR98-485.

Figure 5 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vif [SEQ ID NO: 3] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vif protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR98-485.

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Figure 6 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vpr [SEQ ID NO: 4] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vpr protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 7 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV tat [SEQ ID NO: 5] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV tat protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 8 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV rev [SEQ ID NO: 6] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV rev protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 9 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vpu [SEQ ID NO: 7] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vpu protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 10 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV env [SEQ ID NO: 8] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade

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consensus sequences for the HIV env protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

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Figure 11 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV nef [SEQ ID NO: 9] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV nef protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 12 is a diagrammatic representation depicting the systematic segmentation of the designed degenerate consensus sequences for each HIV protein and the reverse translation of each segment into a DNA sequence. Also shown is the number of segments used during random rearrangement and amino acids that were removed. Amino acids surrounded by an open square were removed from the design, because degenerate codons to cater for the desired amino acid combination required too many degenerate bases to comply with the incorporation of degenerate sequence rules outlined in the description of the invention herein. Amino acids surrounded by an open circle were removed only in the segment concerned mainly because they were coded for in an oligonucleotide overlap region. Amino acids marked with an asterisk were designed differently in one fragment compared to the corresponding overlap region (see tat gene)

Figure 13 is a diagrammatic representation showing the first and second most frequently used codons in mammals used to reverse translate HIV protein segments. Also shown are all first and second most frequently used degenerate codons for two amino acids where only one base is varied. Codons used where more than one base was varied were worked out in each case by comparing all the codons for each amino acid. The IUPAC codes for degenerate bases are also shown.

Figure 14 illustrates the construction plan for the HIV Savine showing the approximate sizes of the subcassettes, cassettes and full-length Savine cDNA and the restriction sites involved in joining them together. Also shown are the extra sequences

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added onto each subcassette during their design and a brief description of how the subcassettes, cassettes and full length cDNA were constructed and transferred into appropriate DNA plasmids. Description of full length construction: pA was cleaved with XhoI/SaII and cloned into XhoI arms of the B cassette; pAB was cleaved with XhoI and cloned into XhoI arms of the C cassette; full length construct is excisable with either XbaI/BamHI at the 5' end or BgIII at the 3' end. Options for excising cassettes: A) XbaI/BamHI at the 5' end, BgIII/XhoI at the 3' end; B) XbaI/BamHI at the 5' end, BgIII/SaII at the 3' end; C) XbaI/BamHI at the 5' end, BgIII/SaII at the 3' end. Cleaving plasmid vectors: pDNAVacc is cleavable with XbaI/XhoI (DNA vaccination); pBCB07 or pTK7.5 vectors are cleavable with BamHI/SaII (Recombinant Vaccinia); pAvipox vector pAF09 is cleavable with BamHI/SaII (Recombinant Avipox).

Figure 15 shows the full length DNA (17253 bp) and protein sequence (5742 aas) of the HIV Savine construct. Fragment boundaries are shown, together with the position of each fragment in each designed HIV protein, fragment number (in brackets), spacer residues (two alanine residues) and which fragment the spacer was for (open boxes and arrows). The location of residual restriction site joining sequences corresponding to subcassette or cassette boundaries (shaded boxes) are also shown, along with start and stop codons, Kozak sequence, the location of the murine influenza virus CTL epitope sequence (near the 3' end), important restriction sites at each end and the position of each degenerate amino acid (indicated by 'X').

Figure 16 depicts the layout and position of oligonucleotides in the designed DNA sequence for subcassette A1. The sequences which anneal to the short amplification oligonucleotides are indicated by hatched boxes and the position of oligonucleotide overlap regions are dark shaded.

Figure 17: Panel (a) depicts the stepwise asymmetric PCR of the two halves of subcassette A1 (lanes 2-5 and 7-9, respectively) and final splicing together by SOEing (lane 10). DNA standards in lane 1 are pUC18 digested with Sau3AI. Panel (b) shows the stepwise ligation-mediated joining and PCR amplification of each cassette as indicated. DNA standards in lane 1 are SPP1 cut with EcoRI.

Figure 18: Panel (a) shows summary of the construction of the DNA vaccine plasmids that express one HIV Savine cassette. Panel (b) shows a summary of the

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construction of the plasmids used for marker rescue recombination to generate Vaccinia viruses expressing one HIV Savine cassette. Panel (c) shows a summary of the construction of the DNA vaccine plasmids which each express a version of the full-length HIV Savine cDNA

Figure 19 shows restimulation of HIV specific polyclonal CTL responses from three HIV-infected patients by the HIV Savine constructs. PBMCs from three different patients were restimulated for 7 days by infection with Vaccinia virus pools expressing the HIV Savine cassettes: Pool 1 included VV-AC1 and VV-BC1; Pool 2 included VV-AC2, VV-BC2 and VV-CC2. The restimulated PBMCs were then mixed with autologous LCLs (effector to target ratio of 50:1), which were either uninfected or infected with either Vaccinia viruses expressing the HIV proteins gag (VV-gag), env (VV-env) or pol (VVpol), VV- HIV Savine pools 1 (light bars) or 2 (dark bars) or a control Vaccinia virus (VV-Lac) and the amount of ⁵¹Cr released used to determine percent specific lysis. K562 cells were used to determine the level of NK cell-mediated killing in their stimulated culture.

Figure 20 is a diagrammatic representation showing CD4+ proliferation of PBMCs from HIV-1 infected patients restimulated with either Pool1 or Pool2 of the HIV-1 Savine. Briefly PBMCs were stained with CFSE and culture for 6 days with or without VVs encoding either pool1 or pool2 of the HIV-1 Savine. Restimulated Cells were then labelled with antibodies and analysed by FACS.

Figure 21 is a graphical representation showing the CTL response in mice vaccinated with the HIV Savine. C57BL6 mice were immunised with the HIV-1 Savine DNA vaccine comprising the six plasmids described in Figure 18a (100 μ g total DNA was given as 50 µg/leg i.m.). One week later Poxviruses (1x10⁷ pfu) comprising Pool 1 of the HIV-1 Savine were used to boost the immune responses. Three weeks later splenocytes from these mice were restimulated with VV-Pool 1 or VV-Pool 2 for 5 days and the resultant effectors used in a 51Cr release cytotoxicity assay against targets infected with CTRVV, VV-pools or VV expressing the natural antigens from HIV-1.

Figure 22 shows immune responses of HIV Immune Macaques (vaccinated with recombinant FPV expressing gag-pol and challenged with HIV-1 2 years prior to experiment). Monkeys 1 and 2 were immunised once at day 0 with VV Savine pool 1 (Three VVs which together express the entire HIV Savine). Monkey 3 was immunised

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twice with FPV-gag-pol *i.e.*, Day 0 is 3 weeks after first FPV-gag-pol immunisation. A) IFN-y detection by ELISPOT of whole blood (0.5 mL, venous blood heparinanticoagulated) stimulated with Aldrithiol-2 inactivated whole HIV-1 (20 hours, 20 μg/mL). Plasma samples were then centrifuged (1000xg) and assayed in duplicate for antigen-specific IFN using capture ELISA. B) Flow cytometric detection of HIV-1 specific CD69+/CD8+ T cells. Freshly isolated PBMCs were stimulated with inactivated HIV-1 as above for 16 hours, washed and labelled with the antibodies. Cells were then analysed using a FACScaliburTM flow cytometer and data. analysed using Cell-Quest software. C) Flow cytometric detection of HIV-1 specific CD69+/CD4+ T cells carried out as in B).

Figure 23 shows a diagram of a system used to carry out the instructions encoded by the storage medium of Figures 28 and 29.

Figure 24 depicts a flow diagram showing an embodiment of a method for designing synthetic polynucleotide and synthetic polypeptides of the invention.

Figure 25 shows an algorithm, which *inter alia* utilises the steps of the method shown in Figure 24.

Figure 26 shows an example of applying the algorithm of Figure 25 to an input consensus polyprotein sequence of Hepatitis C 1a to execute the segmentation of the polyprotein sequence, the rearrangement of the segments, the linkage of the rearranged segments and the outputting of synthetic polynucleotide and polypeptide sequences for the preparation of Savines for treating and/or preventing Hepatitis C infection.

Figure 27 illustrates an example of applying the algorithm of Figure 25 to input consensus melanocyte differentiation antigens (gp100, MART, TRP-1, Tyros, Trp-2, MC1R, MUC1F and MUC1R) and to consensus melanoma specific antigens (BAGE, GAGE-1, gp100ln4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b and LAGE1) to facilitate segmentation of those sequences, to rearrange the segments, to link the rearranged segments and to synthetic polynucleotide and polypeptide sequences for the preparation of Savines for treating and/or preventing melanoma.

Figure 28 shows a cross section of a magnetic storage medium.

Figure 29 shows a cross section of an optically readable data storage medium.



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Figure 30 shows six HIV Savine cassette sequences (A1 [SEQ ID NO: 393], A2 [SEQ ID NO: 399], B1[SEQ ID NO: 395], B2 [SEQ ID NO: 401], C1 [SEQ ID NO: 397] and C2 [SEQ ID NO: 403]). A1, B1 and C1 can be joined together using, for example, convenient restriction enzyme sites provided at the ends of each cassette to construct an embodiment of a full length HIV Savine [SEQ ID NO: 405]. A2, B2 and C2 can also be joined together to provide another embodiment of a full length HIV Savine with 350 aa mutations common in major HIV clades. The cassettes A/B/C can be joined into single constructs using specific restriction enzyme sites incorporated after the start codon or before the stop codon in the cassettes

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BRIEF DESCRIPTION OF THE SEQUENCES: SUMMARY TABLE

TABLE A

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER	959 6 0 mm / 642	: 235,002.11
SEQ ID NO: 1	GAG consensus polypeptide	499 aa
SEQ ID NO: 2	POL consensus polypeptide	995 aa
SEQ ID NO: 3	VIF consensus polypeptide	192 aa
SEQ ID NO: 4	VPR consensus polypeptide	96 aa
SEQ ID NO: 5	TAT consensus polypeptide	102 aa
SEQ ID NO: 6	REV consensus polypeptide	123 aa
SEQ ID NO: 7	VPU consensus polypeptide	81 aa
SEQ ID NO: 8	ENV consensus polypeptide	651 aa
SEQ ID NO: 9	NEF consensus polypeptide	206 aa
SEQ ID NO: 10	GAG segment 1	90 nts
SEQ ID NO: 11	Polypeptide encoded by SEQ ID NO: 10	30 aa
SEQ ID NO: 12	GAG segment 2	90 nts
SEQ ID NO: 13	Polypeptide encoded by SEQ ID NO: 12	30 aa
SEQ ID NO: 14	GAG segment 3	90 nts
SEQ ID NO: 15	Polypeptide encoded by SEQ ID NO: 14	30 aa
SEQ ID NO: 16	GAG segment 4	90 nts
SEQ ID NO: 17	Polypeptide encoded by SEQ ID NO: 16	30 aa
SEQ ID NO: 18	GAG segment 5	90 nts
SEQ ID NO: 19	Polypeptide encoded by SEQ ID NO: 18	30 aa
SEQ ID NO: 20	GAG segment 6	90 nts
SEQ ID NO: 21	Polypeptide encoded by SEQ ID NO: 20	30 aa
SEQ ID NO: 22	GAG segment 7	90 nts

		SZ SPONIZACIONI SI
SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 23	Polypeptide encoded by SEQ ID NO: 22	30 aa
SEQ ID NO: 24	GAG segment 8	90 nts
SEQ ID NO: 25	Polypeptide encoded by SEQ ID NO: 24	30 aa
SEQ ID NO: 26	GAG segment 9	90 nts
SEQ ID NO: 27	Polypeptide encoded by SEQ ID NO: 26	30 aa
SEQ ID NO: 28	GAG segment 10	90 nts
SEQ ID NO: 29	Polypeptide encoded by SEQ ID NO: 28	30 aa
SEQ ID NO: 30	GAG segment 11	90 nts
SEQ ID NO: 31	Polypeptide encoded by SEQ ID NO: 30	30 aa
SEQ ID NO: 32	GAG segment 12	90 nts
SEQ ID NO: 33	Polypeptide encoded by SEQ ID NO: 32	30 aa
SEQ ID NO: 34	GAG segment 13	90 nts
SEQ ID NO: 35	Polypeptide encoded by SEQ ID NO: 34	30 aa
SEQ ID NO: 36	GAG segment 14	90 nts
SEQ ID NO: 37	Polypeptide encoded by SEQ ID NO: 36	30 aa
SEQ ID NO: 38	GAG segment 15	90 nts
SEQ ID NO: 39	Polypeptide encoded by SEQ ID NO: 38	30 aa
SEQ ID NO: 40	GAG segment 16	90 nts
SEQ ID NO: 41	Polypeptide encoded by SEQ ID NO: 40	30 aa
SEQ ID NO: 42	GAG segment 17	90 nts
SEQ ID NO: 43	Polypeptide encoded by SEQ ID NO: 42	30 aa
SEQ ID NO: 44	GAG segment 18	90 nts
SEQ ID NO: 45	Polypeptide encoded by SEQ ID NO: 44	30 aa
SEQ ID NO: 46	GAG segment 19	90 nts

	CEAN TENIAL	LENGTH
SEQUENCE ID NUMBER	SEQUENCE	ILYENVOJI IN
SEQ ID NO: 47	Polypeptide encoded by SEQ ID NO: 46	30 aa
SEQ ID NO: 48	GAG segment 20	90 nts
SEQ ID NO: 49	Polypeptide encoded by SEQ ID NO: 48	30 aa
SEQ ID NO: 50	GAG segment 21	90 nts
SEQ ID NO: 51	Polypeptide encoded by SEQ ID NO: 50	30 aa
SEQ ID NO: 52	GAG segment 22	90 nts
SEQ ID NO: 53	Polypeptide encoded by SEQ ID NO: 52	30 aa
SEQ ID NO: 54	GAG segment 23	90 nts
SEQ ID NO: 55	Polypeptide encoded by SEQ ID NO: 54	30 aa
SEQ ID NO: 56	GAG segment 24	90 nts
SEQ ID NO: 57	Polypeptide encoded by SEQ ID NO: 56	30 aa
SEQ ID NO: 58	GAG segment 25	90 nts
SEQ ID NO: 59	Polypeptide encoded by SEQ ID NO: 58	30 aa
SEQ ID NO: 60	GAG segment 26	90 nts
SEQ ID NO: 61	Polypeptide encoded by SEQ ID NO: 60	30 aa
SEQ ID NO: 62	GAG segment 27	90 nts
SEQ ID NO: 63	Polypeptide encoded by SEQ ID NO: 62	30 aa
SEQ ID NO: 64	GAG segment 28	90 nts
SEQ ID NO: 65	Polypeptide encoded by SEQ ID NO: 64	30 aa
SEQ ID NO: 66	GAG segment 29	90 nts
SEQ ID NO: 67	Polypeptide encoded by SEQ ID NO: 66	30 aa
SEQ ID NO: 68	GAG segment 30	90 nts
SEQ ID NO: 69	Polypeptide encoded by SEQ ID NO: 68	30 aa
SEQ ID NO: 70	GAG segment 31	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 71	Polypeptide encoded by SEQ ID NO: 70	30 aa
SEQ ID NO: 72	GAG segment 32	90 nts
SEQ ID NO: 73	Polypeptide encoded by SEQ ID NO: 72	30 aa
SEQ ID NO: 74	GAG segment 33	57 nts
SEQ ID NO: 75	Polypeptide encoded by SEQ ID NO: 74	19 aa
SEQ ID NO: 76	POL segment 1	90 nts
SEQ ID NO: 77	Polypeptide encoded by SEQ ID NO: 76	30 aa
SEQ ID NO: 78	POL segment 2	90 nts
SEQ ID NO: 79	Polypeptide encoded by SEQ ID NO: 78	30 aa
SEQ ID NO: 80	POL segment 3	90 nts
SEQ ID NO: 81	Polypeptide encoded by SEQ ID NO: 80	30 aa
SEQ ID NO: 82	POL segment 4	90 nts
SEQ ID NO: 83	Polypeptide encoded by SEQ ID NO: 82	30 aa
SEQ ID NO: 84	POL segment 5	90 nts
SEQ ID NO: 85	Polypeptide encoded by SEQ ID NO: 84	30 aa
SEQ ID NO: 86	POL segment 6	90 nts
SEQ ID NO: 87	Polypeptide encoded by SEQ ID NO: 86	30 aa
SEQ ID NO: 88	POL segment 7	90 nts
SEQ ID NO: 89	Polypeptide encoded by SEQ ID NO: 88	30 aa
SEQ ID NO: 90	POL segment 8	90 nts
SEQ ID NO: 91	Polypeptide encoded by SEQ ID NO: 90	30 aa
SEQ ID NO: 92	POL segment 9	90 nts
SEQ ID NO: 93	Polypeptide encoded by SEQ ID NO: 92	30 aa
SEQ ID NO: 94	POL segment 10	90 nts

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 95	Polypeptide encoded by SEQ ID NO: 94	30 aa
SEQ ID NO: 96	POL segment 11	90 nts
SEQ ID NO: 97	Polypeptide encoded by SEQ ID NO: 96	30 aa
SEQ ID NO: 98	POL segment 12	90 nts
SEQ ID NO: 99	Polypeptide encoded by SEQ ID NO: 98	30 aa
SEQ ID NO: 100	POL segment 13	90 nts
SEQ ID NO: 101	Polypeptide encoded by SEQ ID NO: 100	30 aa
SEQ ID NO: 102	POL segment 14	90 nts
SEQ ID NO: 103	Polypeptide encoded by SEQ ID NO: 102	30 aa
SEQ ID NO: 104	POL segment 15	90 nts
SEQ ID NO: 105	Polypeptide encoded by SEQ ID NO: 104	30 aa
SEQ ID NO: 106	POL segment 16	90 nts
SEQ ID NO: 107	Polypeptide encoded by SEQ ID NO: 106	30 aa
SEQ ID NO: 108	POL segment 17	90 nts
SEQ ID NO: 109	Polypeptide encoded by SEQ ID NO: 108	30 aa
SEQ ID NO: 110	POL segment 18	90 nts
SEQ ID NO: 111	Polypeptide encoded by SEQ ID NO: 110	30 aa
SEQ ID NO: 112	POL segment 19	90 nts
SEQ ID NO: 113	Polypeptide encoded by SEQ ID NO: 112	30 aa
SEQ ID NO: 114	POL segment 20	90 nts
SEQ ID NO: 115	Polypeptide encoded by SEQ ID NO: 114	30 aa
SEQ ID NO: 116	POL segment 21	90 nts
SEQ ID NO: 117	Polypeptide encoded by SEQ ID NO: 116	30 aa
SEQ ID NO: 118	POL segment 22	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 119	Polypeptide encoded by SEQ ID NO: 118	30 aa
SEQ ID NO: 120	POL segment 23	90 nts
SEQ ID NO: 121	Polypeptide encoded by SEQ ID NO: 120	30 aa
SEQ ID NO: 122	POL segment 24	90 nts
SEQ ID NO: 123	Polypeptide encoded by SEQ ID NO: 122	30 aa
SEQ ID NO: 124	POL segment 25	90 nts
SEQ ID NO: 125	Polypeptide encoded by SEQ ID NO: 124	30 aa
SEQ ID NO: 126	POL segment 26	90 nts
SEQ ID NO: 127	Polypeptide encoded by SEQ ID NO: 126	30 aa
SEQ ID NO: 128	POL segment 27	90 nts
SEQ ID NO: 129	Polypeptide encoded by SEQ ID NO: 128	30 aa
SEQ ID NO: 130	POL segment 28	90 nts
SEQ ID NO: 131	Polypeptide encoded by SEQ ID NO: 130	30 aa
SEQ ID NO: 132	POL segment 29	90 nts
SEQ ID NO: 133	Polypeptide encoded by SEQ ID NO: 132	30 aa
SEQ ID NO: 134	POL segment 30	90 nts
SEQ ID NO: 135	Polypeptide encoded by SEQ ID NO: 134	30 aa
SEQ ID NO: 136	POL segment 31	90 nts
SEQ ID NO: 137	Polypeptide encoded by SEQ ID NO: 136	30 aa
SEQ ID NO: 138	POL segment 32	90 nts
SEQ ID NO: 139	Polypeptide encoded by SEQ ID NO: 138	30 aa
SEQ ID NO: 140	POL segment 33	90 nts
SEQ ID NO: 141	Polypeptide encoded by SEQ ID NO: 140	30 aa
SEQ ID NO: 142	POL segment 34	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 143	Polypeptide encoded by SEQ ID NO: 142	30 aa
SEQ ID NO: 144	POL segment 35	90 nts
SEQ ID NO: 145	Polypeptide encoded by SEQ ID NO: 144	30 aa
SEQ ID NO: 146	POL segment 36	90 nts
SEQ ID NO: 147	Polypeptide encoded by SEQ ID NO: 146	30 aa
SEQ ID NO: 148	POL segment 37	90 nts
SEQ ID NO: 149	Polypeptide encoded by SEQ ID NO: 148	30 aa
SEQ ID NO: 150	POL segment 38	90 nts
SEQ ID NO: 151	Polypeptide encoded by SEQ ID NO: 150	30 aa
SEQ ID NO: 152	POL segment 39	90 nts
SEQ ID NO: 153	Polypeptide encoded by SEQ ID NO: 152	30 aa
SEQ ID NO: 154	POL segment 40	90 nts
SEQ ID NO: 155	Polypeptide encoded by SEQ ID NO: 154	30 aa
SEQ ID NO: 156	POL segment 41	90 nts
SEQ ID NO: 157	Polypeptide encoded by SEQ ID NO: 156	30 aa
SEQ ID NO: 158	POL segment 42	90 nts
SEQ ID NO: 159	Polypeptide encoded by SEQ ID NO: 158	30 aa
SEQ ID NO: 160	POL segment 43	90 nts
SEQ ID NO: 161	Polypeptide encoded by SEQ ID NO: 160	30 aa
SEQ ID NO: 162	POL segment 44	90 nts
SEQ ID NO: 163	Polypeptide encoded by SEQ ID NO: 162	30 aa
SEQ ID NO: 164	POL segment 45	90 nts
SEQ ID NO: 165	Polypeptide encoded by SEQ ID NO: 164	30 aa
SEQ ID NO: 166	POL segment 46	90 nts

	γ_A	
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SEQUENCE ID NUMBER	SEQUENCE	LIENGTH
SEQ ID NO: 167	Polypeptide encoded by SEQ ID NO: 166	30 aa
SEQ ID NO: 168	POL segment 47	90 nts
SEQ ID NO: 169	Polypeptide encoded by SEQ ID NO: 168	30 aa
SEQ ID NO: 170	POL segment 48	90 nts
SEQ ID NO: 171	Polypeptide encoded by SEQ ID NO: 170	30 aa
SEQ ID NO: 172	POL segment 49	90 nts
SEQ ID NO: 173	Polypeptide encoded by SEQ ID NO: 172	30 aa
SEQ ID NO: 174	POL segment 50	90 nts
SEQ ID NO: 175	Polypeptide encoded by SEQ ID NO: 174	30 aa
SEQ ID NO: 176	POL segment 51	90 nts
SEQ ID NO: 177	Polypeptide encoded by SEQ ID NO: 176	30 aa
SEQ ID NO: 178	POL segment 52	90 nts
SEQ ID NO: 179	Polypeptide encoded by SEQ ID NO: 178	30 aa
SEQ ID NO: 180	POL segment 53	90 nts
SEQ ID NO: 181	Polypeptide encoded by SEQ ID NO: 180	30 aa
SEQ ID NO: 182	POL segment 54	90 nts
SEQ ID NO: 183	Polypeptide encoded by SEQ ID NO: 182	30 aa
SEQ ID NO: 184	POL segment 55	90 nts
SEQ ID NO: 185	Polypeptide encoded by SEQ ID NO: 184	30 aa
SEQ ID NO: 186	POL segment 56	90 nts
SEQ ID NO: 187	Polypeptide encoded by SEQ ID NO: 186	30 aa
SEQ ID NO: 188	POL segment 57	90 nts
SEQ ID NO: 189	Polypeptide encoded by SEQ ID NO: 188	30 aa
SEQ ID NO: 190	POL segment 58	90 nts

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 191	Polypeptide encoded by SEQ ID NO: 190	30 aa
SEQ ID NO: 192	POL segment 59	90 nts
SEQ ID NO: 193	Polypeptide encoded by SEQ ID NO: 192	30 aa
SEQ ID NO: 194	POL segment 60	90 nts
SEQ ID NO: 195	Polypeptide encoded by SEQ ID NO: 194	30 aa
SEQ ID NO: 196	POL segment 61	90 nts
SEQ ID NO: 197	Polypeptide encoded by SEQ ID NO: 196	30 aa
SEQ ID NO: 198	POL segment 62	90 nts
SEQ ID NO: 199	Polypeptide encoded by SEQ ID NO: 198	30 aa
SEQ ID NO: 200	POL segment 63	90 nts
SEQ ID NO: 201	Polypeptide encoded by SEQ ID NO: 200	30 aa
SEQ ID NO: 202	POL segment 64	90 nts
SEQ ID NO: 203	Polypeptide encoded by SEQ ID NO: 202	30 aa
SEQ ID NO: 204	POL segment 65	90 nts
SEQ ID NO: 205	Polypeptide encoded by SEQ ID NO: 204	30 aa
SEQ ID NO: 206	POL segment 66	60 nts
SEQ ID NO: 207	Polypeptide encoded by SEQ ID NO: 206	20 aa
SEQ ID NO: 208	VIF segment 1	90 nts
SEQ ID NO: 209	Polypeptide encoded by SEQ ID NO: 208	30 aa
SEQ ID NO: 210	VIF segment 2	90 nts
SEQ ID NO: 211	Polypeptide encoded by SEQ ID NO: 210	30 aa
SEQ ID NO: 212	VIF segment 3	90 nts
SEQ ID NO: 213	Polypeptide encoded by SEQ ID NO: 212	30 aa
SEQ ID NO: 214	VIF segment 4	90 nts



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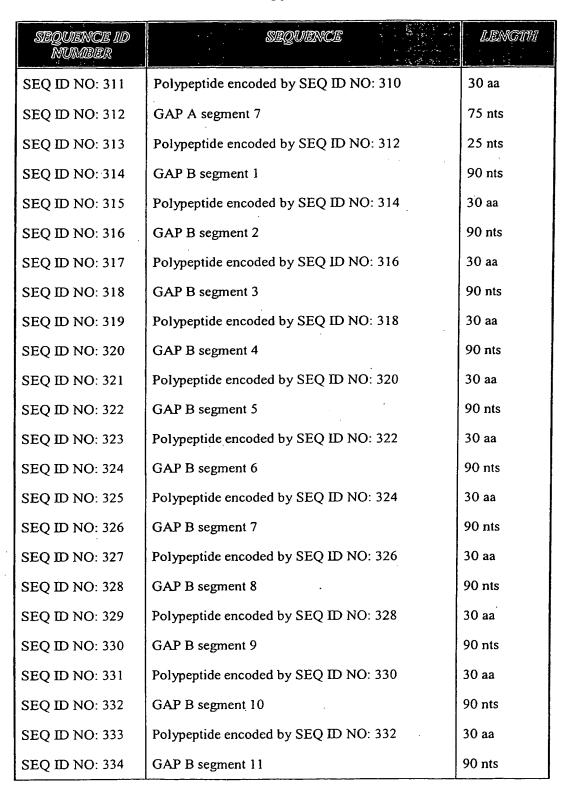
SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 215	Polypeptide encoded by SEQ ID NO: 214	30 aa
SEQ ID NO: 216	VIF segment 5	90 nts
SEQ ID NO: 217	Polypeptide encoded by SEQ ID NO: 216	30 aa
SEQ ID NO: 218	VIF segment 6	90 nts
SEQ ID NO: 219	Polypeptide encoded by SEQ ID NO: 218	30 aa
SEQ ID NO: 220	VIF segment 7	90 nts
SEQ ID NO: 221	Polypeptide encoded by SEQ ID NO: 220	30 aa
SEQ ID NO: 222	VIF segment 8	90 nts
SEQ ID NO: 223	Polypeptide encoded by SEQ ID NO: 222	30 aa
SEQ ID NO: 224	VIF segment 9	90 nts
SEQ ID NO: 225	Polypeptide encoded by SEQ ID NO: 224	30 aa
SEQ ID NO: 226	VIF segment 10	90 nts
SEQ ID NO: 227	Polypeptide encoded by SEQ ID NO: 226	30 aa
SEQ ID NO: 228	VIF segment 11	90 nts
SEQ ID NO: 229	Polypeptide encoded by SEQ ID NO: 228	30 aa
SEQ ID NO: 230	VIF segment 12	81 nts
SEQ ID NO: 231	Polypeptide encoded by SEQ ID NO: 230	27 aa
SEQ ID NO: 232	VPR segment 1	90 nts
SEQ ID NO: 233	Polypeptide encoded by SEQ ID NO: 232	30 aa
SEQ ID NO: 234	VPR segment 2	90 nts
SEQ ID NO: 235	Polypeptide encoded by SEQ ID NO: 234	30 aa
SEQ ID NO: 236	VPR segment 3	90 nts
SEQ ID NO: 237	Polypeptide encoded by SEQ ID NO: 236	30 aa
SEQ ID NO: 238	VPR segment 4	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LIENGTH
SEQ ID NO: 239	Polypeptide encoded by SEQ ID NO: 238	30 aa
SEQ ID NO: 240	VPR segment 5	90 nts
SEQ ID NO: 241	Polypeptide encoded by SEQ ID NO: 240	30 aa
SEQ ID NO: 242	VPR segment 6	63 nts
SEQ ID NO: 243	Polypeptide encoded by SEQ ID NO: 242	21 aa
SEQ ID NO: 244	TAT segment 1	90 nts
SEQ ID NO: 245	Polypeptide encoded by SEQ ID NO: 244	30 aa
SEQ ID NO: 246	TAT segment 2	90 nts
SEQ ID NO: 247	Polypeptide encoded by SEQ ID NO: 246	30 aa
SEQ ID NO: 248	TAT segment 3	90 nts
SEQ ID NO: 249	Polypeptide encoded by SEQ ID NO: 248	30 aa
SEQ ID NO: 250	TAT segment 4	90 nts
SEQ ID NO: 251	Polypeptide encoded by SEQ ID NO: 250	30 aa
SEQ ID NO: 252	TAT segment 5	90 nts
SEQ ID NO: 253	Polypeptide encoded by SEQ ID NO: 252	30 aa
SEQ ID NO: 254	TAT segment 6	81 nts
SEQ ID NO: 255	Polypeptide encoded by SEQ ID NO: 254	27 aa
SEQ ID NO: 256	REV segment 1	90 nts
SEQ ID NO: 257	Polypeptide encoded by SEQ ID NO: 256	30 aa
SEQ ID NO: 258	REV segment 2	90 nts
SEQ ID NO: 259	Polypeptide encoded by SEQ ID NO: 258	30 aa
SEQ ID NO: 260	REV segment 3	90 nts
SEQ ID NO: 261	Polypeptide encoded by SEQ ID NO: 260	30 aa
SEQ ID NO: 262	REV segment 4	90 nts

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SEQUENCE ID	SEQUENCE	LENGTH
NUMBER	Section 1997 And Section 1997 Address And Section 1997 An	
SEQ ID NO: 263	Polypeptide encoded by SEQ ID NO: 262	30 aa
SEQ ID NO: 264	REV segment 5	90 nts
SEQ ID NO: 265	Polypeptide encoded by SEQ ID NO: 264	30 aa
SEQ ID NO: 266	REV segment 6	90 nts
SEQ ID NO: 267	Polypeptide encoded by SEQ ID NO: 266	30 aa
SEQ ID NO: 268	REV segment 7	90 nts
SEQ ID NO: 269	Polypeptide encoded by SEQ ID NO: 268	30 aa
SEQ ID NO: 270	REV segment 8	54 nts
SEQ ID NO: 271	Polypeptide encoded by SEQ ID NO: 270	18 aa
SEQ ID NO: 272	VPU segment 1	90 nts
SEQ ID NO: 273	Polypeptide encoded by SEQ ID NO: 272	30 aa
SEQ ID NO: 274	VPU segment 2	90 nts
SEQ ID NO: 275	Polypeptide encoded by SEQ ID NO: 274	30 aa
SEQ ID NO: 276	VPU segment 3	90 nts
SEQ ID NO: 277	Polypeptide encoded by SEQ ID NO: 276	30 aa
SEQ ID NO: 278	VPU segment 4	90 nts
SEQ ID NO: 279	Polypeptide encoded by SEQ ID NO: 278	30 aa
SEQ ID NO: 280	VPU segment 5	63 nts
SEQ ID NO: 281	Polypeptide encoded by SEQ ID NO: 280	21 aa
SEQ ID NO: 282	ENV segment 1	90 nts
SEQ ID NO: 283	Polypeptide encoded by SEQ ID NO: 282	30 aa
SEQ ID NO: 284	ENV segment 2	90 nts
SEQ ID NO: 285	Polypeptide encoded by SEQ ID NO: 284	30 aa
SEQ ID NO: 286	ENV segment 3	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 287	Polypeptide encoded by SEQ ID NO: 286	30 aa
SEQ ID NO: 288	ENV segment 4	90 nts
SEQ ID NO: 289	Polypeptide encoded by SEQ ID NO: 288	30 aa
SEQ ID NO: 290	ENV segment 5	90 nts
SEQ ID NO: 291	Polypeptide encoded by SEQ ID NO: 290	30 aa
SEQ ID NO: 292	ENV segment 6	90 nts
SEQ ID NO: 293	Polypeptide encoded by SEQ ID NO: 292	30 aa
SEQ ID NO: 294	ENV segment 7	90 nts
SEQ ID NO: 295	Polypeptide encoded by SEQ ID NO: 294	30 aa
SEQ ID NO: 296	ENV segment 8	90 nts
SEQ ID NO: 297	Polypeptide encoded by SEQ ID NO: 296	30 aa
SEQ ID NO: 298	ENV segment 9	57 nts
SEQ ID NO: 299	Polypeptide encoded by SEQ ID NO: 298	19 aa
SEQ ID NO: 300	GAP A segment 1	90 nts
SEQ ID NO: 301	Polypeptide encoded by SEQ ID NO: 300	30 aa
SEQ ID NO: 302	GAP A segment 2	90 nts
SEQ ID NO: 303	Polypeptide encoded by SEQ ID NO: 302	30 aa
SEQ ID NO: 304	GAP A segment 3	90 nts
SEQ ID NO: 305	Polypeptide encoded by SEQ ID NO: 304	30 aa
SEQ ID NO: 306	GAP A segment 4	90 nts
SEQ ID NO: 307	Polypeptide encoded by SEQ ID NO: 306	30 aa
SEQ ID NO: 308	GAP A segment 5	90 nts
SEQ ID NO: 309	Polypeptide encoded by SEQ ID NO: 308	30 aa
SEQ ID NO: 310	GAP A segment 6	90 nts



SEQUENCE ID NUMBER	SEQUENCE	ILENGTH
SEQ ID NO: 335	Polypeptide encoded by SEQ ID NO: 334	30 aa
SEQ ID NO: 336	GAP B segment 12	90 nts .
SEQ ID NO: 337	Polypeptide encoded by SEQ ID NO: 336	30 aa
SEQ ID NO: 338	GAP B segment 13	90 nts
SEQ ID NO: 339	Polypeptide encoded by SEQ ID NO: 338	30 aa
SEQ ID NO: 340	GAP B segment 14	90 nts
SEQ ID NO: 341	Polypeptide encoded by SEQ ID NO: 340	30 aa
SEQ ID NO: 342	GAP B segment 15	90 nts
SEQ ID NO: 343	Polypeptide encoded by SEQ ID NO: 342	30 aa
SEQ ID NO: 344	GAP B segment 16	90 nts
SEQ ID NO: 345	Polypeptide encoded by SEQ ID NO: 344	30 aa
SEQ ID NO: 346	GAP B segment 17	90 nts
SEQ ID NO: 347	Polypeptide encoded by SEQ ID NO: 346	30 aa
SEQ ID NO: 348	GAP B segment 18	90 nts
SEQ ID NO: 349	Polypeptide encoded by SEQ ID NO: 348	30 aa
SEQ ID NO: 350	GAP B segment 19	90 nts
SEQ ID NO: 351	Polypeptide encoded by SEQ ID NO: 350	30 aa
SEQ ID NO: 352	GAP B segment 20	90 nts
SEQ ID NO: 353	Polypeptide encoded by SEQ ID NO: 352	30 aa
SEQ ID NO: 354	GAP B segment 21	90 nts
SEQ ID NO: 355	Polypeptide encoded by SEQ ID NO: 354	30 aa
SEQ ID NO: 356	GAP B segment 22	90 nts
SEQ ID NO: 357	Polypeptide encoded by SEQ ID NO: 356	30 aa
SEQ ID NO: 358	GAP B segment 23	90 nts



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 359	Polypeptide encoded by SEQ ID NO: 358	30 aa
SEQ ID NO: 360	GAP B segment 24	90 nts
SEQ ID NO: 361	Polypeptide encoded by SEQ ID NO: 360	30 aa
SEQ ID NO: 362	GAP B segment 25	90 nts
SEQ ID NO: 363	Polypeptide encoded by SEQ ID NO: 362	30 aa
SEQ ID NO: 364	GAP B segment 26	66 nts
SEQ ID NO: 365	Polypeptide encoded by SEQ ID NO: 364	22 aa
SEQ ID NO: 366	NEF segment 1	90 nts
SEQ ID NO: 367	Polypeptide encoded by SEQ ID NO: 366	30 aa
SEQ ID NO: 368	NEF segment 2	90 nts
SEQ ID NO: 369	Polypeptide encoded by SEQ ID NO: 368	30 aa
SEQ ID NO: 370	NEF segment 3	90 nts
SEQ ID NO: 371	Polypeptide encoded by SEQ ID NO: 370	30 aa
SEQ ID NO: 372	NEF segment 4	90 nts
SEQ ID NO: 373	Polypeptide encoded by SEQ ID NO: 372	30 aa
SEQ ID NO: 374	NEF segment 5	90 nts
SEQ ID NO: 375	Polypeptide encoded by SEQ ID NO: 374	30 aa
SEQ ID NO: 376	NEF segment 6	90 nts
SEQ ID NO: 377	Polypeptide encoded by SEQ ID NO: 376	30 aa
SEQ ID NO: 378	NEF segment 7	90 nts
SEQ ID NO: 379	Polypeptide encoded by SEQ ID NO: 378	30 aa
SEQ ID NO: 380	NEF segment 8	90 nts
SEQ ID NO: 381	Polypeptide encoded by SEQ ID NO: 380	30 aa
SEQ ID NO: 382	NEF segment 9	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 383	Polypeptide encoded by SEQ ID NO: 382	30 aa
SEQ ID NO: 384	NEF segment 10	90 nts
SEQ ID NO: 385	Polypeptide encoded by SEQ ID NO: 384	30 aa
SEQ ID NO: 386	NEF segment 11	90 nts
SEQ ID NO: 387	Polypeptide encoded by SEQ ID NO: 386	30 aa
SEQ ID NO: 388	NEF segment 12	90 nts
SEQ ID NO: 389	Polypeptide encoded by SEQ ID NO: 388	30 aa
SEQ ID NO: 390	NEF segment 13	78 nts
SEQ ID NO: 391	Polypeptide encoded by SEQ ID NO: 390	26 aa
SEQ ID NO: 392	HIV Cassette A1	5703 nts
SEQ ID NO: 393	Polypeptide encoded by SEQ ID NO:392	1896 aa
SEQ ID NO: 394	HIV Cassette B1	5685 nts
SEQ ID NO: 395	Polypeptide encoded by SEQ ID NO: 394	1890 aa
SEQ ID NO: 396	HIV Cassette C1	5925 nts
SEQ ID NO: 397	Polypeptide encoded by SEQ ID NO: 396	1967 aa
SEQ ID NO: 398	HIV Cassette A2	5703 nts
SEQ ID NO: 399	Polypeptide encoded by SEQ ID NO: 398	1896 aa
SEQ ID NO: 400	HIV Cassette B2	5685 nts
SEQ ID NO: 401	Polypeptide encoded by SEQ ID NO: 400	1890 aa
SEQ ID NO: 402	HIV Cassette C2	5925 nts
SEQ ID NO: 403	Polypeptide encoded by SEQ ID NO: 402	1967 aa
SEQ ID NO: 404	HIV complete Savine	17244 nts
SEQ ID NO: 405	Polypeptide encoded by SEQ ID NO: 404	5747 aa
SEQ ID NO: 406	HepCla consensus polyprotein sequence	3011 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 407	HepCla segment 1	90 nts
SEQ ID NO: 408	Polypeptide encoded by SEQ ID NO: 407	30 aa
SEQ ID NO: 409	HepCla segment 2	90 nts
SEQ ID NO: 410	Polypeptide encoded by SEQ ID NO: 409	30 aa
SEQ ID NO: 411	HepCla segment 3	90 nts
SEQ ID NO: 412	Polypeptide encoded by SEQ ID NO: 411	30 aa
SEQ ID NO: 413	HepCla segment 4	90 nts
SEQ ID NO: 414	Polypeptide encoded by SEQ ID NO: 413	30 aa
SEQ ID NO: 415	HepCla segment 5	90 nts
SEQ ID NO: 416	Polypeptide encoded by SEQ ID NO: 415	30 aa
SEQ ID NO: 417	HepCla segment 6	90 nts
SEQ ID NO: 418	Polypeptide encoded by SEQ ID NO: 417	30 aa
SEQ ID NO: 419	HepCla segment 7	90 nts
SEQ ID NO: 420	Polypeptide encoded by SEQ ID NO: 419	30 aa
SEQ ID NO: 421	HepCla segment 8	90 nts
SEQ ID NO: 422	Polypeptide encoded by SEQ ID NO: 421	30 aa
SEQ ID NO: 423	HepCla segment 9	90 nts
SEQ ID NO: 424	Polypeptide encoded by SEQ ID NO: 423	30 aa
SEQ ID NO: 425	HepCla segment 10	90 nts
SEQ ID NO: 426	Polypeptide encoded by SEQ ID NO: 425	30 aa
SEQ ID NO: 427	HepCla segment 11	90 nts
SEQ ID NO: 428	Polypeptide encoded by SEQ ID NO: 427	30 aa
SEQ ID NO: 429	HepCla segment 12	90 nts
SEQ ID NO: 430	Polypeptide encoded by SEQ ID NO: 429	30 aa

	SEQUENCE	LENGTH
SEQUENCE ID NUMBER		יוטי זו שאיאנענ
SEQ ID NO: 431	HepCla segment 13	90 nts
SEQ ID NO: 432	Polypeptide encoded by SEQ ID NO: 431	30 aa
SEQ ID NO: 433	HepCla segment 14	90 nts
SEQ ID NO: 434	Polypeptide encoded by SEQ ID NO: 433	30 aa
SEQ ID NO: 435	HepCla segment 15	90 nts
SEQ ID NO: 436	Polypeptide encoded by SEQ ID NO: 435	30 aa
SEQ ID NO: 437	HepCla segment 16	90 nts
SEQ ID NO: 438	Polypeptide encoded by SEQ ID NO: 437	30 aa
SEQ ID NO: 439	HepCla segment 17	90 nts
SEQ ID NO: 440	Polypeptide encoded by SEQ ID NO: 439	30 aa
SEQ ID NO: 441	HepCla segment 18	90 nts
SEQ ID NO: 442	Polypeptide encoded by SEQ ID NO: 441	30 aa
SEQ ID NO: 443	HepCla segment 19	90 nts
SEQ ID NO: 444	Polypeptide encoded by SEQ ID NO: 443	30 aa
SEQ ID NO: 445	HepCla segment 20	90 nts
SEQ ID NO: 446	Polypeptide encoded by SEQ ID NO: 445	30 aa
SEQ ID NO: 447	HepCla segment 21	90 nts
SEQ ID NO: 448	Polypeptide encoded by SEQ ID NO: 447	30 aa
SEQ ID NO: 449	HepC1a segment 22	90 nts
SEQ ID NO: 450	Polypeptide encoded by SEQ ID NO: 449	30 aa
SEQ ID NO: 451	HepCla segment 23	90 nts
SEQ ID NO: 452	Polypeptide encoded by SEQ ID NO: 451	30 aa
SEQ ID NO: 453	HepCla segment 24	90 nts
SEQ ID NO: 454	Polypeptide encoded by SEQ ID NO: 453	30 aa



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 455	HepCla segment 25	90 nts
SEQ ID NO: 456	Polypeptide encoded by SEQ ID NO: 455	30 aa
SEQ ID NO: 457	HepCla segment 26	90 nts
SEQ ID NO: 458	Polypeptide encoded by SEQ ID NO: 457	30 aa
SEQ ID NO: 459	HepCla segment 27	90 nts
SEQ ID NO: 460	Polypeptide encoded by SEQ ID NO: 459	30 aa
SEQ ID NO: 461	HepCla segment 28	90 nts
SEQ ID NO: 462	Polypeptide encoded by SEQ ID NO: 461	30 aa
SEQ ID NO: 463	HepCla segment 29	90 nts
SEQ ID NO: 464	Polypeptide encoded by SEQ ID NO: 463	30 aa
SEQ ID NO: 465	HepCla segment 30	90 nts
SEQ ID NO: 466	Polypeptide encoded by SEQ ID NO: 465	30 aa
SEQ ID NO: 467	HepCla segment 31	90 nts
SEQ ID NO: 468	Polypeptide encoded by SEQ ID NO: 467	30 aa
SEQ ID NO: 469	HepC1a segment 32	90 nts
SEQ ID NO: 470	Polypeptide encoded by SEQ ID NO: 469	30 aa
SEQ ID NO: 471	HepCla segment 33	90 nts
SEQ ID NO: 472	Polypeptide encoded by SEQ ID NO: 471	30 aa
SEQ ID NO: 473	HepCla segment 34	90 nts
SEQ ID NO: 474	Polypeptide encoded by SEQ ID NO: 473	30 aa
SEQ ID NO: 475	HepCla segment 35	90 nts
SEQ ID NO: 476	Polypeptide encoded by SEQ ID NO: 475	30 aa
SEQ ID NO: 477	HepCla segment 36	90 nts
SEQ ID NO: 478	Polypeptide encoded by SEQ ID NO: 477	30 aa

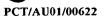
SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 479	HepC1a segment 37	90 nts
SEQ ID NO: 480	Polypeptide encoded by SEQ ID NO: 479	30 aa
SEQ ID NO: 481	HepC1a segment 38	90 nts
SEQ ID NO: 482	Polypeptide encoded by SEQ ID NO: 481	30 aa
SEQ ID NO: 483	HepC1a segment 39	90 nts
SEQ ID NO: 484	Polypeptide encoded by SEQ ID NO: 483	30 aa
SEQ ID NO: 485	HepC1a segment 40	90 nts
SEQ ID NO: 486	Polypeptide encoded by SEQ ID NO: 485	30 aa
SEQ ID NO: 487	HepCla segment 41	90 nts
SEQ ID NO: 488	Polypeptide encoded by SEQ ID NO: 487	30 aa
SEQ ID NO: 489	HepC1a segment 42	90 nts
SEQ ID NO: 490	Polypeptide encoded by SEQ ID NO: 489	30 aa
SEQ ID NO: 491	HepCla segment 43	90 nts
SEQ ID NO: 492	Polypeptide encoded by SEQ ID NO: 491	30 aa
SEQ ID NO: 493	HepCla segment 44	90 nts
SEQ ID NO: 494	Polypeptide encoded by SEQ ID NO: 493	30 aa
SEQ ID NO: 495	HepCla segment 45	90 nts
SEQ ID NO: 496	Polypeptide encoded by SEQ ID NO: 495	30 aa
SEQ ID NO: 497	HepCla segment 46	90 nts
SEQ ID NO: 498	Polypeptide encoded by SEQ ID NO: 497	30 aa
SEQ ID NO: 499	HepCla segment 47	90 nts
SEQ ID NO: 500	Polypeptide encoded by SEQ ID NO: 499	30 aa
SEQ ID NO: 501	HepCla segment 48	90 nts
SEQ ID NO: 502	Polypeptide encoded by SEQ ID NO: 501	30 aa



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 503	HepCla segment 49	90 nts
SEQ ID NO: 504	Polypeptide encoded by SEQ ID NO: 503	30 aa
SEQ ID NO: 505	HepC1a segment 50	90 nts
SEQ ID NO: 506	Polypeptide encoded by SEQ ID NO: 505	30 aa
SEQ ID NO: 507	HepCla segment 51	90 nts
SEQ ID NO: 508	Polypeptide encoded by SEQ ID NO: 507	30 aa
SEQ ID NO: 509	HepCla segment 52	90 nts
SEQ ID NO: 510	Polypeptide encoded by SEQ ID NO: 509	30 aa
SEQ ID NO: 511	HepC1a segment 53	90 nts
SEQ ID NO: 512	Polypeptide encoded by SEQ ID NO: 511	30 aa
SEQ ID NO: 513	HepCla segment 54	90 nts
SEQ ID NO: 514	Polypeptide encoded by SEQ ID NO: 513	30 aa
SEQ ID NO: 515	HepCla segment 55	90 nts
SEQ ID NO: 516	Polypeptide encoded by SEQ ID NO: 515	30 aa
SEQ ID NO: 517	HepCla segment 56	90 nts
SEQ ID NO: 518	Polypeptide encoded by SEQ ID NO: 517	30 aa
SEQ ID NO: 519	HepCla segment 57	90 nts
SEQ ID NO: 520	Polypeptide encoded by SEQ ID NO: 519	30 aa
SEQ ID NO: 521	HepCla segment 58	90 nts
SEQ ID NO: 522	Polypeptide encoded by SEQ ID NO: 521	30 aa
SEQ ID NO: 523	HepCla segment 59	90 nts
SEQ ID NO: 524	Polypeptide encoded by SEQ ID NO: 523	30 aa
SEQ ID NO: 525	HepC1a segment 60	90 nts
SEQ ID NO: 526	Polypeptide encoded by SEQ ID NO: 525	30 aa

SEQUIENCE ID NUMBER	. SEQUENCE	LENGTH
SEQ ID NO: 527	HepCla segment 61	90 nts
SEQ ID NO: 528	Polypeptide encoded by SEQ ID NO: 527	30 aa
SEQ ID NO: 529	HepCla segment 62	90 nts
SEQ ID NO: 530	Polypeptide encoded by SEQ ID NO: 529	30 aa
SEQ ID NO: 531	HepCla segment 63	90 nts
SEQ ID NO: 532	Polypeptide encoded by SEQ ID NO: 531	30 aa
SEQ ID NO: 533	HepCla segment 64	90 nts
SEQ ID NO: 534	Polypeptide encoded by SEQ ID NO: 533	30 aa
SEQ ID NO: 535	HepCla segment 65	90 nts
SEQ ID NO: 536	Polypeptide encoded by SEQ ID NO: 535	30 aa
SEQ ID NO: 537	HepCla segment 66	90 nts
SEQ ID NO: 538	Polypeptide encoded by SEQ ID NO: 537	30 aa
SEQ ID NO: 539	HepCla segment 67	90 nts
SEQ ID NO: 540	Polypeptide encoded by SEQ ID NO: 539	30 aa
SEQ ID NO: 541	HepCla segment 68	90 nts
SEQ ID NO: 542	Polypeptide encoded by SEQ ID NO: 541	30 aa
SEQ ID NO: 543	HepCla segment 69	90 nts
SEQ ID NO: 544	Polypeptide encoded by SEQ ID NO: 543	30 aa
SEQ ID NO: 545	HepCla segment 70	90 nts
SEQ ID NO: 546	Polypeptide encoded by SEQ ID NO:545	30 aa
SEQ ID NO: 547	HepCla segment 71	90 nts
SEQ ID NO: 548	Polypeptide encoded by SEQ ID NO: 547	30 aa
SEQ ID NO: 549	HepCla segment 72	90 nts
SEQ ID NO: 550	Polypeptide encoded by SEQ ID NO: 549	30 aa



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 551	HepCla segment 73	90 nts
SEQ ID NO: 552	Polypeptide encoded by SEQ ID NO: 551	30 aa
SEQ ID NO: 553	HepCla segment 74	90 nts
SEQ ID NO: 554	Polypeptide encoded by SEQ ID NO: 553	30 aa
SEQ ID NO: 555	HepCla segment 75	90 nts
SEQ ID NO: 556	Polypeptide encoded by SEQ ID NO: 555	30 aa
SEQ ID NO: 557	HepCla segment 76	90 nts
SEQ ID NO: 558	Polypeptide encoded by SEQ ID NO: 557	30 aa
SEQ ID NO: 559	HepCla segment 77	90 nts
SEQ ID NO: 560	Polypeptide encoded by SEQ ID NO: 559	30 aa
SEQ ID NO: 561	HepCla segment 78	90 nts
SEQ ID NO: 562	Polypeptide encoded by SEQ ID NO: 561	30 aa
SEQ ID NO: 563	HepCla segment 79	90 nts
SEQ ID NO: 564	Polypeptide encoded by SEQ ID NO: 563	30 aa
SEQ ID NO: 565	HepCla segment 80	90 nts
SEQ ID NO: 566	Polypeptide encoded by SEQ ID NO: 565	30 aa
SEQ ID NO: 567	HepCla segment 81	90 nts
SEQ ID NO: 568	Polypeptide encoded by SEQ ID NO: 567	30 aa
SEQ ID NO: 569	HepCla segment 82	90 nts
SEQ ID NO: 570	Polypeptide encoded by SEQ ID NO: 569	30 aa
SEQ ID NO: 571	HepCla segment 83	90 nts
SEQ ID NO: 572	Polypeptide encoded by SEQ ID NO: 571	30 aa
SEQ ID NO: 573	HepCla segment 84	90 nts
SEQ ID NO: 574	Polypeptide encoded by SEQ ID NO: 573	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 575	HepC1a segment 85	90 nts
SEQ ID NO: 576	Polypeptide encoded by SEQ ID NO: 575	30 aa
SEQ ID NO: 577	HepC1a segment 86	90 nts
SEQ ID NO: 578	Polypeptide encoded by SEQ ID NO: 577	30 aa
SEQ ID NO: 579	HepC1a segment 87	90 nts
SEQ ID NO: 580	Polypeptide encoded by SEQ ID NO: 579	30 aa
SEQ ID NO: 581	HepCla segment 88	90 nts
SEQ ID NO: 582	Polypeptide encoded by SEQ ID NO: 581	30 aa
SEQ ID NO: 583	HepCla segment 89	90 nts
SEQ ID NO: 584	Polypeptide encoded by SEQ ID NO: 583	30 aa
SEQ ID NO: 585	HepCla segment 90	90 nts
SEQ ID NO: 586	Polypeptide encoded by SEQ ID NO: 585	30 aa
SEQ ID NO: 587	HepCla segment 91	90 nts
SEQ ID NO: 588	Polypeptide encoded by SEQ ID NO: 587	30 aa
SEQ ID NO: 589	HepCla segment 92	90 nts
SEQ ID NO: 590	Polypeptide encoded by SEQ ID NO: 589	30 aa
SEQ ID NO: 591	HepCla segment 93	90 nts
SEQ ID NO: 592	Polypeptide encoded by SEQ ID NO: 591	30 aa
SEQ ID NO: 593	HepCla segment 94	90 nts
SEQ ID NO: 594	Polypeptide encoded by SEQ ID NO: 593	30 aa
SEQ ID NO: 595	HepCla segment 95	90 nts
SEQ ID NO: 596	Polypeptide encoded by SEQ ID NO: 595	30 aa
SEQ ID NO: 597	HepCla segment 96	90 nts
SEQ ID NO: 598	Polypeptide encoded by SEQ ID NO: 597	30 aa

SEQUENCE IID NUMBIR	SEQUENCE	LENGTH
SEQ ID NO: 599	HepC1a segment 97	90 nts
SEQ ID NO: 600	Polypeptide encoded by SEQ ID NO: 599	30 aa
SEQ ID NO: 601	HepCla segment 98	90 nts
SEQ ID NO: 602	Polypeptide encoded by SEQ ID NO: 601	30 aa
SEQ ID NO: 603	HepCla segment 99	90 nts
SEQ ID NO: 604	Polypeptide encoded by SEQ ID NO: 603	30 aa
SEQ ID NO: 605	HepCla segment 100	90 nts
SEQ ID NO: 606	Polypeptide encoded by SEQ ID NO: 605	30 aa
SEQ ID NO: 607	HepCla segment 101	90 nts
SEQ ID NO: 608	Polypeptide encoded by SEQ ID NO: 607	30 aa
SEQ ID NO: 609	HepCla segment 102	90 nts
SEQ ID NO: 610	Polypeptide encoded by SEQ ID NO: 609	30 aa
SEQ ID NO: 611	HepCla segment 103	90 nts
SEQ ID NO: 612	Polypeptide encoded by SEQ ID NO: 611	30 aa
SEQ ID NO: 613	HepCla segment 104	90 nts
SEQ ID NO: 614	Polypeptide encoded by SEQ ID NO: 613	30 aa
SEQ ID NO: 615	HepCla segment 105	90 nts
SEQ ID NO: 616	Polypeptide encoded by SEQ ID NO: 615	30 aa
SEQ ID NO: 617	HepCla segment 106	90 nts
SEQ ID NO: 618	Polypeptide encoded by SEQ ID NO: 617	30 aa
SEQ ID NO: 619	HepCla segment 107	90 nts
SEQ ID NO: 620	Polypeptide encoded by SEQ ID NO: 619	30 aa
SEQ ID NO: 621	HepCla segment 108	90 nts
SEQ ID NO: 622	Polypeptide encoded by SEQ ID NO: 621	30 aa

SEQUIENCE IID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 623	HepCla segment 109	90 nts
SEQ ID NO: 624	Polypeptide encoded by SEQ ID NO: 623	30 aa
SEQ ID NO: 625	HepCla segment 110	90 nts
SEQ ID NO: 626	Polypeptide encoded by SEQ ID NO: 625	30 aa
SEQ ID NO: 627	HepCla segment 111	90 nts
SEQ ID NO: 628	Polypeptide encoded by SEQ ID NO: 627	30 aa
SEQ ID NO: 629	HepC1a segment 112	90 nts
SEQ ID NO: 630	Polypeptide encoded by SEQ ID NO: 629	30 aa
SEQ ID NO: 631	HepCla segment 113	90 nts
SEQ ID NO: 632	Polypeptide encoded by SEQ ID NO: 631	30 aa
SEQ ID NO: 633	HepCla segment 114	90 nts
SEQ ID NO: 634	Polypeptide encoded by SEQ ID NO: 633	30 aa
SEQ ID NO: 635	HepCla segment 115	90 nts
SEQ ID NO: 636	Polypeptide encoded by SEQ ID NO: 635	30 aa
SEQ ID NO: 637	HepCla segment 116	90 nts
SEQ ID NO: 638	Polypeptide encoded by SEQ ID NO: 637	30 aa
SEQ ID NO: 639	HepCla segment 117	90 nts
SEQ ID NO: 640	Polypeptide encoded by SEQ ID NO: 639	30 aa
SEQ ID NO: 641	HepCla segment 118	90 nts
SEQ ID NO: 642	Polypeptide encoded by SEQ ID NO: 641	30 aa
SEQ ID NO: 643	HepCla segment 119	90 nts
SEQ ID NO: 644	Polypeptide encoded by SEQ ID NO: 643	30 aa
SEQ ID NO: 645	HepCla segment 120	90 nts
SEQ ID NO: 646	Polypeptide encoded by SEQ ID NO: 645	30 aa



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SEQUENCE ID	SEQUENCE	ILENGTH
NUMBER	<u>මපති</u> මකාලය	22010201
SEQ ID NO: 647	HepC1a segment 121	90 nts
SEQ ID NO: 648	Polypeptide encoded by SEQ ID NO: 647	30 aa
SEQ ID NO: 649	HepC1a segment 122	90 nts
SEQ ID NO: 650	Polypeptide encoded by SEQ ID NO: 649	30 aa
SEQ ID NO: 651	HepC1a segment 123	90 nts
SEQ ID NO: 652	Polypeptide encoded by SEQ ID NO: 651	30 aa
SEQ ID NO: 653	HepC1a segment 124	90 nts
SEQ ID NO: 654	Polypeptide encoded by SEQ ID NO: 653	30 aa
SEQ ID NO: 655	HepC1a segment 125	90 nts
SEQ ID NO: 656	Polypeptide encoded by SEQ ID NO: 655	30 aa
SEQ ID NO: 657	HepCla segment 126	90 nts
SEQ ID NO: 658	Polypeptide encoded by SEQ ID NO: 657	30 aa
SEQ ID NO: 659	HepC1a segment 127	90 nts
SEQ ID NO: 660	Polypeptide encoded by SEQ ID NO: 659	30 aa
SEQ ID NO: 661	HepCla segment 128	90 nts
SEQ ID NO: 662	Polypeptide encoded by SEQ ID NO: 661	30 aa
SEQ ID NO: 663	HepC1a segment 129	90 nts
SEQ ID NO: 664	Polypeptide encoded by SEQ ID NO: 663	30 aa
SEQ ID NO: 665	HepCla segment 130	90 nts
SEQ ID NO: 666	Polypeptide encoded by SEQ ID NO: 665	30 aa
SEQ ID NO: 667	HepCla segment 131	90 nts
SEQ ID NO: 668	Polypeptide encoded by SEQ ID NO: 667	30 aa
SEQ ID NO: 669	HepCla segment 132	90 nts
SEQ ID NO: 670	Polypeptide encoded by SEQ ID NO: 669	30 aa

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SEQUENCE ID	SEQUENCE	LENGTH
NUMBER	· · · · · · · · · · · · · · · · · · ·	
SEQ ID NO: 671	HepC1a segment 133	90 nts
SEQ ID NO: 672	Polypeptide encoded by SEQ ID NO: 671	30 aa
SEQ ID NO: 673	HepC1a segment 134	90 nts
SEQ ID NO: 674	Polypeptide encoded by SEQ ID NO: 673	30 aa
SEQ ID NO: 675	HepC1a segment 135	90 nts
SEQ ID NO: 676	Polypeptide encoded by SEQ ID NO: 675	30 aa
SEQ ID NO: 677	HepCla segment 136	90 nts
SEQ ID NO: 678	Polypeptide encoded by SEQ ID NO: 677	30 aa
SEQ ID NO: 679	HepCla segment 137	90 nts
SEQ ID NO: 680	Polypeptide encoded by SEQ ID NO: 679	30 aa
SEQ ID NO: 681	HepC1a segment 138	90 nts
SEQ ID NO: 682	Polypeptide encoded by SEQ ID NO: 681	30 aa
SEQ ID NO: 683	HepCla segment 139	90 nts
SEQ ID NO: 684	Polypeptide encoded by SEQ ID NO: 683	30 aa
SEQ ID NO: 685	HepC1a segment 140	90 nts
SEQ ID NO: 686	Polypeptide encoded by SEQ ID NO: 685	30 aa
SEQ ID NO: 687	HepCla segment 141	90 nts
SEQ ID NO: 688	Polypeptide encoded by SEQ ID NO: 687	30 aa
SEQ ID NO: 689	HepC1a segment 142	90 nts
SEQ ID NO: 690	Polypeptide encoded by SEQ ID NO: 689	30 aa
SEQ ID NO: 691	HepCla segment 143	90 nts
SEQ ID NO: 692	Polypeptide encoded by SEQ ID NO: 691	30 aa
SEQ ID NO: 693	HepCla segment 144	90 nts
SEQ ID NO: 694	Polypeptide encoded by SEQ ID NO: 693	30 aa

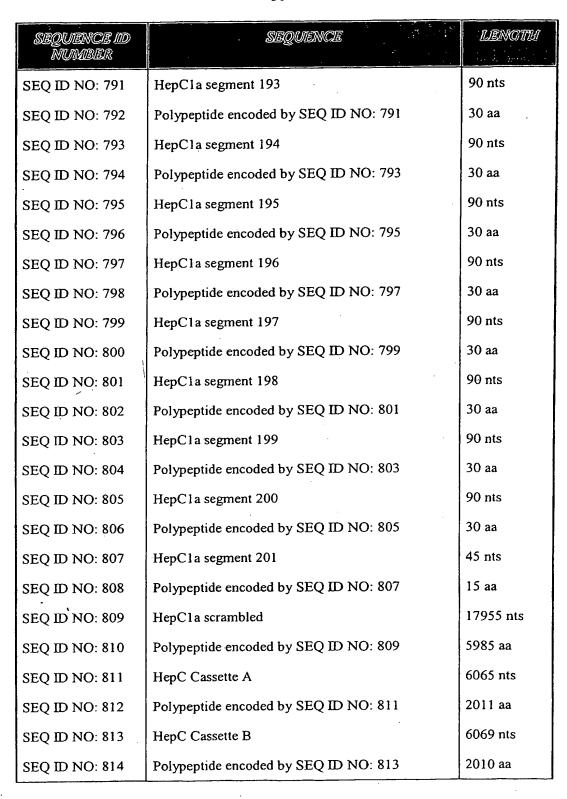
SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 695	HepC1a segment 145	90 nts
SEQ ID NO: 696	Polypeptide encoded by SEQ ID NO: 695	30 aa
SEQ ID NO: 697	HepCla segment 146	90 nts
SEQ ID NO: 698	Polypeptide encoded by SEQ ID NO: 697	30 aa
SEQ ID NO: 699	HepCla segment 147	90 nts
SEQ ID NO: 700	Polypeptide encoded by SEQ ID NO: 699	30 aa
SEQ ID NO: 701	HepCla segment 148	90 nts
SEQ ID NO: 702	Polypeptide encoded by SEQ ID NO: 701	30 aa
SEQ ID NO: 703	HepCla segment 149	90 nts
SEQ ID NO: 704	Polypeptide encoded by SEQ ID NO: 703	30 aa
SEQ ID NO: 705	HepCla segment 150	90 nts
SEQ ID NO: 706	Polypeptide encoded by SEQ ID NO: 705	30 aa
SEQ ID NO: 707	HepCla segment 151	90 nts
SEQ ID NO: 708	Polypeptide encoded by SEQ ID NO: 707	30 aa
SEQ ID NO: 709	HepCla segment 152	90 nts
SEQ ID NO: 710	Polypeptide encoded by SEQ ID NO: 709	30 aa
SEQ ID NO: 711	HepC1a segment 153	90 nts
SEQ ID NO: 712	Polypeptide encoded by SEQ ID NO: 711	30 aa
SEQ ID NO: 713	HepCla segment 154	90 nts
SEQ ID NO: 714	Polypeptide encoded by SEQ ID NO: 713	30 aa
SEQ ID NO: 715	HepCla segment 155	90 nts
SEQ ID NO: 716	Polypeptide encoded by SEQ ID NO: 715	30 aa
SEQ ID NO: 717	HepCla segment 156	90 nts
SEQ ID NO: 718	Polypeptide encoded by SEQ ID NO: 717	30 aa

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		7 (50) 26 (50) I
SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 719	HepCla segment 157	90 nts
SEQ ID NO: 720	Polypeptide encoded by SEQ ID NO: 719	30 aa
SEQ ID NO: 721	HepCla segment 158	90 nts
SEQ ID NO: 722	Polypeptide encoded by SEQ ID NO: 721	30 aa
SEQ ID NO: 723	HepCla segment 159	90 nts
SEQ ID NO: 724	Polypeptide encoded by SEQ ID NO: 723	30 aa
SEQ ID NO: 725	HepCla segment 160	90 nts
SEQ ID NO: 726	Polypeptide encoded by SEQ ID NO: 725	30 aa
SEQ ID NO: 727	HepCla segment 161	90 nts
SEQ ID NO: 728	Polypeptide encoded by SEQ ID NO: 727	30 aa
SEQ ID NO: 729	HepCla segment 162	90 nts
SEQ ID NO: 730	Polypeptide encoded by SEQ ID NO: 729	30 aa
SEQ ID NO: 731	HepCla segment 163	90 nts
SEQ ID NO: 732	Polypeptide encoded by SEQ ID NO: 731	30 aa
SEQ ID NO: 733	HepCla segment 164	90 nts
SEQ ID NO: 734	Polypeptide encoded by SEQ ID NO: 733	30 aa
SEQ ID NO: 735	HepCla segment 165	90 nts
SEQ ID NO: 736	Polypeptide encoded by SEQ ID NO: 735	30 aa
SEQ ID NO: 737	HepCla segment 166	90 nts
SEQ ID NO: 738	Polypeptide encoded by SEQ ID NO: 737	30 aa
SEQ ID NO: 739	HepCla segment 167	90 nts
SEQ ID NO: 740	Polypeptide encoded by SEQ ID NO: 739	30 aa
SEQ ID NO: 741	HepCla segment 168	90 nts
SEQ ID NO: 742	Polypeptide encoded by SEQ ID NO: 741	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 743	HepCla segment 169	90 nts
SEQ ID NO: 744	Polypeptide encoded by SEQ ID NO: 743	30 aa
SEQ ID NO: 745	HepCla segment 170	90 nts
SEQ ID NO: 746	Polypeptide encoded by SEQ ID NO: 745	30 aa
SEQ ID NO: 747	HepCla segment 171	90 nts
SEQ ID NO: 748	Polypeptide encoded by SEQ ID NO: 747	30 aa
SEQ ID NO: 749	HepCla segment 172	90 nts
SEQ ID NO: 750	Polypeptide encoded by SEQ ID NO: 749	30 aa
SEQ ID NO: 751	HepCla segment 173	90 nts
SEQ ID NO: 752	Polypeptide encoded by SEQ ID NO: 751	30 aa
SEQ ID NO: 753	HepCla segment 174	90 nts
SEQ ID NO: 754	Polypeptide encoded by SEQ ID NO: 753	30 aa
SEQ ID NO: 755	HepCla segment 175	90 nts
SEQ ID NO: 756	Polypeptide encoded by SEQ ID NO: 755	30 aa
SEQ ID NO: 757	HepCla segment 176	90 nts
SEQ ID NO: 758	Polypeptide encoded by SEQ ID NO: 757	30 aa
SEQ ID NO: 759	HepCla segment 177	90 nts
SEQ ID NO: 760	Polypeptide encoded by SEQ ID NO: 759	30 aa
SEQ ID NO: 761	HepCla segment 178	90 nts
SEQ ID NO: 762	Polypeptide encoded by SEQ ID NO: 761	30 aa
SEQ ID NO: 763	HepCla segment 179	90 nts
SEQ ID NO: 764	Polypeptide encoded by SEQ ID NO: 763	30 aa
SEQ ID NO: 765	HepCla segment 180	90 nts
SEQ ID NO: 766	Polypeptide encoded by SEQ ID NO: 765	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER	MEGA CIBIA CE	799 <u>3</u> 80 © 5 11 11
SEQ ID NO: 767	HepCla segment 181	90 nts
SEQ ID NO: 768	Polypeptide encoded by SEQ ID NO: 767	30 aa
SEQ ID NO: 769	HepCla segment 182	90 nts
SEQ ID NO: 770	Polypeptide encoded by SEQ ID NO: 769	30 aa
SEQ ID NO: 771	HepCla segment 183	90 nts
SEQ ID NO: 772	Polypeptide encoded by SEQ ID NO: 771	-30 aa
SEQ ID NO: 773	HepCla segment 184	90 nts
SEQ ID NO: 774	Polypeptide encoded by SEQ ID NO: 773	30 aa
SEQ ID NO: 775	HepCla segment 185	90 nts
SEQ ID NO: 776	Polypeptide encoded by SEQ ID NO: 775	30 aa
SEQ ID NO: 777	HepCla segment 186	90 nts
SEQ ID NO: 778	Polypeptide encoded by SEQ ID NO: 777	30 aa
SEQ ID NO: 779	HepCla segment 187	90 nts
SEQ ID NO: 780	Polypeptide encoded by SEQ ID NO: 779	30 aa
SEQ ID NO: 781	HepCla segment 188	90 nts
SEQ ID NO: 782	Polypeptide encoded by SEQ ID NO: 781	30 aa
SEQ ID NO: 783	HepCla segment 189	90 nts
SEQ ID NO: 784	Polypeptide encoded by SEQ ID NO: 783	30 aa
SEQ ID NO: 785	HepCla segment 190	90 nts
SEQ ID NO: 786	Polypeptide encoded by SEQ ID NO: 785	30 aa
SEQ ID NO: 787	HepCla segment 191	90 nts
SEQ ID NO: 788	Polypeptide encoded by SEQ ID NO: 787	30 aa
SEQ ID NO: 789	HepCla segment 192	90 nts
SEQ ID NO: 790	Polypeptide encoded by SEQ ID NO: 789	30 aa



SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 815	HepC Cassette C	6030 nts
SEQ ID NO: 816	Polypeptide encoded by SEQ ID NO: 815	1997 aa
SEQ ID NO: 817	gp100 consensus polypeptide	661 aa
SEQ ID NO: 818	MART consensus polypeptide	118 aa
SEQ ID NO: 819	TRP-1 consensus polypeptide	248 aa
SEQ ID NO: 820	Tyros consensus polypeptide	529 aa
SEQ ID NO: 821	TRP2 consensus polypeptide	519 aa
SEQ ID NO: 822	MC1R consensus polypeptide	317 aa
SEQ ID NO: 823	MUCIF consensus polypeptide	125 aa
SEQ ID NO: 824	MUC1R consensus polypeptide	312 aa
SEQ ID NO: 825	BAGE consensus polypeptide	43 aa
SEQ ID NO: 826	GAGE-1 consensus polypeptide	138 aa
SEQ ID NO: 827	gp100ln4 consensus polypeptide	51 aa
SEQ ID NO: 828	MAGE-1 consensus polypeptide	309 aa
SEQ ID NO: 829	MAGE-3 consensus polypeptide	314 aa
SEQ ID NO: 830	PRAME consensus polypeptide	509 aa
SEQ ID NO: 831	TRP2IN2 consensus polypeptide	54 aa
SEQ ID NO: 832	NYNSO1a consensus polypeptide	180 aa
SEQ ID NO: 833	NYNSO1b consensus polypeptide	58 aa
SEQ ID NO: 834	LAGE1 consensus polypeptide	180 aa
SEQ ID NO: 835	gp100 segment 1	90 nts
SEQ ID NO: 836	Polypeptide encoded by SEQ ID NO: 835	30 aa
SEQ ID NO: 837	gp100 segment 2	90 nts
SEQ ID NO: 838	Polypeptide encoded by SEQ ID NO: 837	30 aa



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 839	gp100 segment 3	90 nts
SEQ ID NO: 840	Polypeptide encoded by SEQ ID NO: 839	30 aa
SEQ ID NO: 841	gp100 segment 4	90 nts
SEQ ID NO: 842	Polypeptide encoded by SEQ ID NO: 841	30 aa
SEQ ID NO: 843	gp100 segment 5	90 nts
SEQ ID NO: 844	Polypeptide encoded by SEQ ID NO: 843	30 aa
SEQ ID NO: 845	gp100 segment 6	90 nts
SEQ ID NO: 846	Polypeptide encoded by SEQ ID NO: 845	30 aa
SEQ ID NO: 847	gp100 segment 7	90 nts
SEQ ID NO: 848	Polypeptide encoded by SEQ ID NO: 847	30 aa
SEQ ID NO: 849	gp100 segment 8	90 nts
SEQ ID NO: 850	Polypeptide encoded by SEQ ID NO: 849	30 aa
SEQ ID NO: 851	gp100 segment 9	90 nts
SEQ ID NO: 852	Polypeptide encoded by SEQ ID NO: 851	30 aa
SEQ ID NO: 853	gp100 segment 10	90 nts
SEQ ID NO: 854	Polypeptide encoded by SEQ ID NO: 853	30 aa
SEQ ID NO: 855	gp100 segment 11	90 nts
SEQ ID NO: 856	Polypeptide encoded by SEQ ID NO: 855	30 aa
SEQ ID NO: 857	gp100 segment 12	90 nts
SEQ ID NO: 858	Polypeptide encoded by SEQ ID NO: 857	30 aa
SEQ ID NO: 859	gp100 segment 13	90 nts
SEQ ID NO: 860	Polypeptide encoded by SEQ ID NO: 859	30 aa
SEQ ID NO: 861	gp100 segment 14	90 nts
SEQ ID NO: 862	Polypeptide encoded by SEQ ID NO: 861	30 aa

SEQUENCE ID NUMBER	SEQUENCE :	LENGTH
SEQ ID NO: 863	gp100 segment 15	90 nts
SEQ ID NO: 864	Polypeptide encoded by SEQ ID NO: 863	30 aa
SEQ ID NO: 865	gp100 segment 16	90 nts
SEQ ID NO: 866	Polypeptide encoded by SEQ ID NO: 865	30 aa
SEQ ID NO: 867	gp100 segment 17	90 nts
SEQ ID NO: 868	Polypeptide encoded by SEQ ID NO: 867	30 aa
SEQ ID NO: 869	gp100 segment 18	90 nts
SEQ ID NO: 870	Polypeptide encoded by SEQ ID NO: 869	30 aa
SEQ ID NO: 871	gp100 segment 19	90 nts
SEQ ID NO: 872	Polypeptide encoded by SEQ ID NO: 871	30 aa
SEQ ID NO: 873	gp100 segment 20	90 nts
SEQ ID NO: 874	Polypeptide encoded by SEQ ID NO: 873	30 aa
SEQ ID NO: 875	gp100 segment 21	90 nts
SEQ ID NO: 876	Polypeptide encoded by SEQ ID NO: 875	30 aa
SEQ ID NO: 877	gp100 segment 22	90 nts
SEQ ID NO: 878	Polypeptide encoded by SEQ ID NO: 877	30 aa
SEQ ID NO: 879	gp100 segment 23	90 nts
SEQ ID NO: 880	Polypeptide encoded by SEQ ID NO: 879	30 aa
SEQ ID NO: 881	gp100 segment 24	90 nts
SEQ ID NO: 882	Polypeptide encoded by SEQ ID NO: 881	30 aa
SEQ ID NO: 883	gp100 segment 25	90 nts
SEQ ID NO: 884	Polypeptide encoded by SEQ ID NO: 883	30 aa
SEQ ID NO: 885	gp100 segment 26	90 nts
SEQ ID NO: 886	Polypeptide encoded by SEQ ID NO: 885	30 aa



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 887	gp100 segment 27	90 nts
SEQ ID NO: 888	Polypeptide encoded by SEQ ID NO: 887	30 aa
SEQ ID NO: 889	gp100 segment 28	90 nts
SEQ ID NO: 890	Polypeptide encoded by SEQ ID NO: 889	30 aa
SEQ ID NO: 891	gp100 segment 29	90 nts
SEQ ID NO: 892	Polypeptide encoded by SEQ ID NO: 891	30 aa
SEQ ID NO: 893	gp100 segment 30	90 nts
SEQ ID NO: 894	Polypeptide encoded by SEQ ID NO: 893	30 aa
SEQ ID NO: 895	gp100 segment 31	90 nts
SEQ ID NO: 896	Polypeptide encoded by SEQ ID NO: 895	30 aa
SEQ ID NO: 897	gp100 segment 32	90 nts
SEQ ID NO: 898	Polypeptide encoded by SEQ ID NO: 897	30 aa
SEQ ID NO: 899	gp100 segment 33	90 nts
SEQ ID NO: 900	Polypeptide encoded by SEQ ID NO: 899	30 aa
SEQ ID NO: 901	gp100 segment 34	90 nts
SEQ ID NO: 902	Polypeptide encoded by SEQ ID NO: 901	30 aa
SEQ ID NO: 903	gp100 segment 35	90 nts
SEQ ID NO: 904	Polypeptide encoded by SEQ ID NO: 903	30 aa
SEQ ID NO: 905	gp100 segment 36	90 nts
SEQ ID NO: 906	Polypeptide encoded by SEQ ID NO: 905	30 aa
SEQ ID NO: 907	gp100 segment 37	90 nts
SEQ ID NO: 908	Polypeptide encoded by SEQ ID NO: 907	30 aa
SEQ ID NO: 909	gp100 segment 38	90 nts
SEQ ID NO: 910	Polypeptide encoded by SEQ ID NO: 909	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 911	gp100 segment 39	90 nts
SEQ ID NO: 912	Polypeptide encoded by SEQ ID NO: 911	30 aa
SEQ ID NO: 913	gp100 segment 40	90 nts
SEQ ID NO: 914	Polypeptide encoded by SEQ ID NO: 913	30 aa
SEQ ID NO: 915	gp100 segment 41	90 nts
SEQ ID NO: 916	Polypeptide encoded by SEQ ID NO: 915	30 aa
SEQ ID NO: 917	gp100 segment 42	90 nts
SEQ ID NO: 918	Polypeptide encoded by SEQ ID NO: 917	30 aa
SEQ ID NO: 919	gp100 segment 43	90 nts
SEQ ID NO: 920	Polypeptide encoded by SEQ ID NO: 919	30 aa
SEQ ID NO: 921	gp100 segment 44	60nts
SEQ ID NO: 922	Polypeptide encoded by SEQ ID NO: 921	20 aa
SEQ ID NO: 923	MART segment 1	90 nts
SEQ ID NO: 924	Polypeptide encoded by SEQ ID NO: 923	30 aa
SEQ ID NO: 925	MART segment 2	90 nts
SEQ ID NO: 926	Polypeptide encoded by SEQ ID NO: 925	30 aa
SEQ ID NO: 927	MART segment 3	90 nts
SEQ ID NO: 928	Polypeptide encoded by SEQ ID NO: 927	30 aa
SEQ ID NO: 929	MART segment 4	90 nts
SEQ ID NO: 930	Polypeptide encoded by SEQ ID NO: 929	30 aa
SEQ ID NO: 931	MART segment 5	90 nts
SEQ ID NO: 932	Polypeptide encoded by SEQ ID NO: 931	30 aa
SEQ ID NO: 933	MART segment 6	90 nts
SEQ ID NO: 934	Polypeptide encoded by SEQ ID NO: 933	30 aa



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 935	MART segment 7	90 nts
SEQ ID NO: 936	Polypeptide encoded by SEQ ID NO: 935	30 aa
SEQ ID NO: 937	MART segment 8	51 nts
SEQ ID NO: 938	Polypeptide encoded by SEQ ID NO: 937	17 aa
SEQ ID NO: 939	trp-1 segment 1	90 nts
SEQ ID NO: 940	Polypeptide encoded by SEQ ID NO: 939	30 aa
SEQ ID NO: 941	trp-1 segment 2	90 nts
SEQ ID NO: 942	Polypeptide encoded by SEQ ID NO: 941	30 aa
SEQ ID NO: 943	trp-1 segment 3	90 nts
SEQ ID NO: 944	Polypeptide encoded by SEQ ID NO: 943	30 aa
SEQ ID NO: 945	trp-1 segment 4	90 nts
SEQ ID NO: 946	Polypeptide encoded by SEQ ID NO: 945	30 aa
SEQ ID NO: 947	trp-1 segment 5	90 nts
SEQ ID NO: 948	Polypeptide encoded by SEQ ID NO: 947	30 aa
SEQ ID NO: 949	trp-1 segment 6	90 nts
SEQ ID NO: 950	Polypeptide encoded by SEQ ID NO: 949	30 aa
SEQ ID NO: 951	trp-1 segment 7	90 nts
SEQ ID NO: 952	Polypeptide encoded by SEQ ID NO: 951	30 aa
SEQ ID NO: 953	trp-1 segment 8	90 nts
SEQ ID NO: 954	Polypeptide encoded by SEQ ID NO: 953	30 aa
SEQ ID NO: 955	trp-1 segment 9	90 nts
SEQ ID NO: 956	Polypeptide encoded by SEQ ID NO: 955	30 aa
SEQ ID NO: 957	trp-1 segment 10	90 nts
SEQ ID NO: 958	Polypeptide encoded by SEQ ID NO: 957	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 959	trp-1 segment 11	90 nts
SEQ ID NO: 960	Polypeptide encoded by SEQ ID NO: 959	30 aa
SEQ ID NO: 961	trp-1 segment 12	90 nts
SEQ ID NO: 962	Polypeptide encoded by SEQ ID NO: 961	30 aa
SEQ ID NO: 963	trp-1 segment 13	90 nts
SEQ ID NO: 964	Polypeptide encoded by SEQ ID NO: 963	30 aa
SEQ ID NO: 965	trp-1 segment 14	90 nts
SEQ ID NO: 966	Polypeptide encoded by SEQ ID NO: 965	30 aa
SEQ ID NO: 967	trp-1 segment 15	90 nts
SEQ ID NO: 968	Polypeptide encoded by SEQ ID NO: 967	30 aa
SEQ ID NO: 969	trp-1 segment 16	81 nts
SEQ ID NO: 970	Polypeptide encoded by SEQ ID NO: 969	27 aa
SEQ ID NO: 971	tyros segment 1	90 nts
SEQ ID NO: 972	Polypeptide encoded by SEQ ID NO: 971	30 aa
SEQ ID NO: 973	tyros segment 2	90 nts
SEQ ID NO: 974	Polypeptide encoded by SEQ ID NO: 973	30 aa
SEQ ID NO: 975	tyros segment 3	90 nts
SEQ ID NO: 976	Polypeptide encoded by SEQ ID NO: 975	30 aa
SEQ ID NO: 977	tyros segment 4	90 nts
SEQ ID NO: 978	Polypeptide encoded by SEQ ID NO: 977	30 aa
SEQ ID NO: 979	tyros segment 5	90 nts
SEQ ID NO: 980	Polypeptide encoded by SEQ ID NO: 979	30 aa
SEQ ID NO: 981	tyros segment 6	90 nts
SEQ ID NO: 982	Polypeptide encoded by SEQ ID NO: 981	30 aa



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 983	tyros segment 7	.90 nts
SEQ ID NO: 984	Polypeptide encoded by SEQ ID NO: 983	30 aa
SEQ ID NO: 985	tyros segment 8	90 nts
SEQ ID NO: 986	Polypeptide encoded by SEQ ID NO: 985	30 aa
SEQ ID NO: 987	tyros segment 9	90 nts
SEQ ID NO: 988	Polypeptide encoded by SEQ ID NO: 987	30 aa
SEQ ID NO: 989	tyros segment 10	90 nts
SEQ ID NO: 990	Polypeptide encoded by SEQ ID NO: 989	30 aa
SEQ ID NO: 991	tyros segment 11	90 nts
SEQ ID NO: 992	Polypeptide encoded by SEQ ID NO: 991	30 aa
SEQ ID NO: 993	tyros segment 12	90 nts
SEQ ID NO: 994	Polypeptide encoded by SEQ ID NO: 993	30 aa
SEQ ID NO: 995	tyros segment 13	90 nts
SEQ ID NO: 996	Polypeptide encoded by SEQ ID NO: 995	30 aa
SEQ ID NO: 997	tyros segment 14	90 nts
SEQ ID NO: 998	Polypeptide encoded by SEQ ID NO: 997	30 aa
SEQ ID NO: 999	tyros segment 15	90 nts
SEQ ID NO: 1000	Polypeptide encoded by SEQ ID NO: 999	30 aa
SEQ ID NO: 1001	tyros segment 16	90 nts
SEQ ID NO: 1002	Polypeptide encoded by SEQ ID NO: 1001	30 aa
SEQ ID NO: 1003	tyros segment 17	90 nts
SEQ ID NO: 1004	Polypeptide encoded by SEQ ID NO: 1003	30 aa
SEQ ID NO: 1005	tyros segment 18	90 nts
SEQ ID NO: 1006	Polypeptide encoded by SEQ ID NO: 1005	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER	\$\$\$\tilde{\tilie}\tilde{\tilde{\tilde{\tilde{\tilde{\tilde{\tilde{\tilde	29.50 V C 11 11 11
SEQ ID NO: 1007	tyros segment 19	90 nts
SEQ ID NO: 1008	Polypeptide encoded by SEQ ID NO: 1007	30 aa
SEQ ID NO: 1009	tyros segment 20	90 nts
SEQ ID NO: 1010	Polypeptide encoded by SEQ ID NO: 1009	30 aa
SEQ ID NO: 1011	tyros segment 21	90 nts
SEQ ID NO: 1012	Polypeptide encoded by SEQ ID NO: 1011	30 aa
SEQ ID NO: 1013	tyros segment 22	90 nts
SEQ ID NO: 1014	Polypeptide encoded by SEQ ID NO: 1013	30 aa
SEQ ID NO: 1015	tyros segment 23	90 nts
SEQ ID NO: 1016	Polypeptide encoded by SEQ ID NO: 1015	30 aa
SEQ ID NO: 1017	tyros segment 24	90 nts
SEQ ID NO: 1018	Polypeptide encoded by SEQ ID NO: 1017	30 aa
SEQ ID NO: 1019	tyros segment 25	90 nts
SEQ ID NO: 1020	Polypeptide encoded by SEQ ID NO: 1019	30 aa
SEQ ID NO: 1021	tyros segment 26	90 nts
SEQ ID NO: 1022	Polypeptide encoded by SEQ ID NO: 1021	30 aa
SEQ ID NO: 1023	tyros segment 27	90 nts
SEQ ID NO: 1024	Polypeptide encoded by SEQ ID NO: 1023	30 aa
SEQ ID NO: 1025	tyros segment 28	90 nts
SEQ ID NO: 1026	Polypeptide encoded by SEQ ID NO: 1025	30 aa
SEQ ID NO: 1027	tyros segment 29	90 nts
SEQ ID NO: 1028	Polypeptide encoded by SEQ ID NO: 1027	30 aa
SEQ ID NO: 1029	tyros segment 30	90 nts
SEQ ID NO: 1030	Polypeptide encoded by SEQ ID NO: 1029	30 aa



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SEQUIENCIE IID MUMBIER	SEQUENCE	LENGTH
SEQ ID NO: 1031	tyros segment 31	90 nts
SEQ ID NO: 1032	Polypeptide encoded by SEQ ID NO: 1031	30 aa
SEQ ID NO: 1033	tyros segment 32	90 nts
SEQ ID NO: 1034	Polypeptide encoded by SEQ ID NO: 1033	30 aa
SEQ ID NO: 1035	tyros segment 33	90 nts
SEQ ID NO: 1036	Polypeptide encoded by SEQ ID NO: 1035	30 aa
SEQ ID NO: 1037	tyros segment 34	90 nts
SEQ ID NO: 1038	Polypeptide encoded by SEQ ID NO: 1037	30 aa
SEQ ID NO: 1039	tyros segment 35	69 nts
SEQ ID NO: 1040	Polypeptide encoded by SEQ ID NO: 1039	23 aa
SEQ ID NO: 1041	trp2 segment 1	90 nts
SEQ ID NO: 1042	Polypeptide encoded by SEQ ID NO: 1041	30 aa
SEQ ID NO: 1043	trp2 segment 2	90 nts
SEQ ID NO: 1044	Polypeptide encoded by SEQ ID NO: 1043	30 aa
SEQ ID NO: 1045	trp2 segment 3	90 nts
SEQ ID NO: 1046	Polypeptide encoded by SEQ ID NO: 1045	30 aa
SEQ ID NO: 1047	trp2 segment 4	90 nts
SEQ ID NO: 1048	Polypeptide encoded by SEQ ID NO: 1047	30 aa
SEQ ID NO: 1049	trp2 segment 5	90 nts
SEQ ID NO: 1050	Polypeptide encoded by SEQ ID NO: 1049	30 aa
SEQ ID NO: 1051	trp2 segment 6	90 nts
SEQ ID NO: 1052	Polypeptide encoded by SEQ ID NO: 1051	30 aa
SEQ ID NO: 1053	trp2 segment 7	90 nts
SEQ ID NO: 1054	Polypeptide encoded by SEQ ID NO: 1053	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1055	trp2 segment 8	90 nts
SEQ ID NO: 1056	Polypeptide encoded by SEQ ID NO: 1055	30 aa
SEQ ID NO: 1057	trp2 segment 9	90 nts
SEQ ID NO: 1058	Polypeptide encoded by SEQ ID NO: 1057	30 aa
SEQ ID NO: 1059	trp2 segment 10	90 nts
SEQ ID NO: 1060	Polypeptide encoded by SEQ ID NO: 1059	30 aa
SEQ ID NO: 1061	trp2 segment 11	90 nts
SEQ ID NO: 1062	Polypeptide encoded by SEQ ID NO: 1061	30 aa
SEQ ID NO: 1063	trp2 segment 12	90 nts
SEQ ID NO: 1064	Polypeptide encoded by SEQ ID NO: 1063	30 aa
SEQ ID NO: 1065	trp2 segment 13	90 nts
SEQ ID NO: 1066	Polypeptide encoded by SEQ ID NO: 1065	30 aa
SEQ ID NO: 1067	trp2 segment 14	90 nts
SEQ ID NO: 1068	Polypeptide encoded by SEQ ID NO: 1067	30 aa
SEQ ID NO: 1069	trp2 segment 15	90 nts
SEQ ID NO: 1070	Polypeptide encoded by SEQ ID NO: 1069	30 aa
SEQ ID NO: 1071	trp2 segment 16	90 nts
SEQ ID NO: 1072	Polypeptide encoded by SEQ ID NO: 1071	30 aa
SEQ ID NO: 1073	trp2 segment 17	90 nts
SEQ ID NO: 1074	Polypeptide encoded by SEQ ID NO: 1073	30 aa
SEQ ID NO: 1075	trp2 segment 18	90 nts
SEQ ID NO: 1076	Polypeptide encoded by SEQ ID NO: 1075	30 aa
SEQ ID NO: 1077	trp2 segment 19	90 nts
SEQ ID NO: 1078	Polypeptide encoded by SEQ ID NO: 1077	30 aa



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SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 1079	trp2 segment 20	90 nts
SEQ ID NO: 1080	Polypeptide encoded by SEQ ID NO: 1079	30 aa
SEQ ID NO: 1081	trp2 segment 21	90 nts
SEQ ID NO: 1082	Polypeptide encoded by SEQ ID NO: 1081	30 aa
SEQ ID NO: 1083	trp2 segment 22	90 nts
SEQ ID NO: 1084	Polypeptide encoded by SEQ ID NO: 1083	30 aa
SEQ ID NO: 1085	trp2 segment 23	90 nts
SEQ ID NO: 1086	Polypeptide encoded by SEQ ID NO: 1085	30 aa
SEQ ID NO: 1087	trp2 segment 24	90 nts
SEQ ID NO: 1088	Polypeptide encoded by SEQ ID NO: 1087	30 aa
SEQ ID NO: 1089	trp2 segment 25	90 nts
SEQ ID NO: 1090	Polypeptide encoded by SEQ ID NO: 1089	30 aa
SEQ ID NO: 1091	trp2 segment 26	90 nts
SEQ ID NO: 1092	Polypeptide encoded by SEQ ID NO: 1091	30 aa
SEQ ID NO: 1093	trp2 segment 27	90 nts
SEQ ID NO: 1094	Polypeptide encoded by SEQ ID NO: 1093	30 aa
SEQ ID NO: 1095	trp2 segment 28	90 nts
SEQ ID NO: 1096	Polypeptide encoded by SEQ ID NO: 1095	30 aa
SEQ ID NO: 1097	trp2 segment 29	90 nts
SEQ ID NO: 1098	Polypeptide encoded by SEQ ID NO: 1097	30 aa
SEQ ID NO: 1099	trp2 segment 30	90 nts
SEQ ID NO: 1100	Polypeptide encoded by SEQ ID NO: 1099	30 aa
SEQ ID NO: 1101	trp2 segment 31	90 nts
SEQ ID NO: 1102	Polypeptide encoded by SEQ ID NO: 1101	30 aa

SEQUIENCE IID MUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1103	trp2 segment 32	90 nts
SEQ ID NO: 1104	Polypeptide encoded by SEQ ID NO: 1103	30 aa
SEQ ID NO: 1105	trp2 segment 33	90 nts
SEQ ID NO: 1106	Polypeptide encoded by SEQ ID NO: 1105	30 aa
SEQ ID NO: 1107	trp2 segment 34	84 nts
SEQ ID NO: 1108	Polypeptide encoded by SEQ ID NO: 1107	28 aa
SEQ ID NO: 1109	MC1R segment 1	90 nts
SEQ ID NO: 1110	Polypeptide encoded by SEQ ID NO: 1109	30 aa
SEQ ID NO: 1111	MC1R segment 2	90 nts
SEQ ID NO: 1112	Polypeptide encoded by SEQ ID NO: 1111	30 aa
SEQ ID NO: 1113	MC1R segment 3	90 nts
SEQ ID NO: 1114	Polypeptide encoded by SEQ ID NO: 1113	30 aa
SEQ ID NO: 1115	MC1R segment 4	90 nts
SEQ ID NO: 1116	Polypeptide encoded by SEQ ID NO: 1115	30 aa
SEQ ID NO: 1117	MC1R segment 5	90 nts
SEQ ID NO: 1118	Polypeptide encoded by SEQ ID NO: 1117	30 aa
SEQ ID NO: 1119	MC1R segment 6	90 nts
SEQ ID NO: 1120	Polypeptide encoded by SEQ ID NO: 1119	30 aa
SEQ ID NO: 1121	MC1R segment 7	90 nts
SEQ ID NO: 1122	Polypeptide encoded by SEQ ID NO: 1121	30 aa
SEQ ID NO: 1123	MC1R segment 8	90 nts
SEQ ID NO: 1124	Polypeptide encoded by SEQ ID NO: 1123	30 aa
SEQ ID NO: 1125	MC1R segment 9	90 nts
SEQ ID NO: 1126	Polypeptide encoded by SEQ ID NO: 1125	30 aa



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1127	MC1R segment 10	90 nts
SEQ ID NO: 1128	Polypeptide encoded by SEQ ID NO: 1127	30 aa
SEQ ID NO: 1129	MC1R segment 11	90 nts
SEQ ID NO: 1130	Polypeptide encoded by SEQ ID NO: 1129	30 aa
SEQ ID NO: 1131	MC1R segment 12	90 nts
SEQ ID NO: 1132	Polypeptide encoded by SEQ ID NO: 1131	30 aa
SEQ ID NO: 1133	MC1R segment 13	90 nts
SEQ ID NO: 1134	Polypeptide encoded by SEQ ID NO: 1133	30 aa
SEQ ID NO: 1135	MC1R segment 14	90 nts
SEQ ID NO: 1136	Polypeptide encoded by SEQ ID NO: 1135	30 aa
SEQ ID NO: 1137	MC1R segment 15	90 nts
SEQ ID NO: 1138	Polypeptide encoded by SEQ ID NO: 1137	30 aa
SEQ ID NO: 1139	MC1R segment 16	90 nts
SEQ ID NO: 1140	Polypeptide encoded by SEQ ID NO: 1139	30 aa
SEQ ID NO: 1141	MC1R segment 17	90 nts
SEQ ID NO: 1142	Polypeptide encoded by SEQ ID NO: 1141	30 aa
SEQ ID NO: 1143	MC1R segment 18	90 nts
SEQ ID NO: 1144	Polypeptide encoded by SEQ ID NO: 1143	30 aa
SEQ ID NO: 1145	MC1R segment 19	90 nts
SEQ ID NO: 1146	Polypeptide encoded by SEQ ID NO: 1145	30 aa
SEQ ID NO: 1147	MC1R segment 20	90 nts
SEQ ID NO: 1148	Polypeptide encoded by SEQ ID NO: 1147	30 aa
SEQ ID NO: 1149	MC1R segment 21	63 nts
SEQ ID NO: 1150	Polypeptide encoded by SEQ ID NO: 1149	21 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1151	MUC1F segment 1	90 nts
SEQ ID NO: 1152	Polypeptide encoded by SEQ ID NO: 1151	30 aa
SEQ ID NO: 1153	MUC1F segment 2	90 nts
SEQ ID NÖ: 1154	Polypeptide encoded by SEQ ID NO: 1153	30 aa
SEQ ID NO: 1155	MUC1F segment 3	90 nts
SEQ ID NO: 1156	Polypeptide encoded by SEQ ID NO: 1155	30 aa
SEQ ID NO: 1157	MUC1F segment 4	90 nts
SEQ ID NO: 1158	Polypeptide encoded by SEQ ID NO: 1157	30 aa
SEQ ID NO: 1159	MUC1F segment 5	90 nts
SEQ ID NO: 1160	Polypeptide encoded by SEQ ID NO: 1159	30 aa
SEQ ID NO: 1161	MUC1F segment 6	90 nts
SEQ ID NO: 1162	Polypeptide encoded by SEQ ID NO: 1161	30 aa
SEQ ID NO: 1163	MUC1F segment 7	90 nts
SEQ ID NO: 1164	Polypeptide encoded by SEQ ID NO: 1163	30 aa
SEQ ID NO: 1165	MUC1F segment 8	72 nts
SEQ ID NO: 1166	Polypeptide encoded by SEQ ID NO: 1165	24 aa
SEQ ID NO: 1167	MUC1R segment 1	90 nts
SEQ ID NO: 1168	Polypeptide encoded by SEQ ID NO: 1167	30 aa
SEQ ID NO: 1169	MUC1R segment 2	90 nts
SEQ ID NO: 1170	Polypeptide encoded by SEQ ID NO: 1169	30 aa
SEQ ID NO: 1171	MUC1R segment 3	90 nts
SEQ ID NO: 1172	Polypeptide encoded by SEQ ID NO: 1171	30 aa
SEQ ID NO: 1173	MUC1R segment 4	90 nts
SEQ ID NO: 1174	Polypeptide encoded by SEQ ID NO: 1173	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1175	MUC1R segment 5	90 nts
SEQ ID NO: 1176	Polypeptide encoded by SEQ ID NO: 1175	30 aa
SEQ ID NO: 1177	MUC1R segment 6	90 nts
SEQ ID NO: 1178	Polypeptide encoded by SEQ ID NO: 1177	30 aa
SEQ ID NO: 1179	MUC1R segment 7	90 nts
SEQ ID NO: 1180	Polypeptide encoded by SEQ ID NO: 1179	30 aa
SEQ ID NO: 1181	MUC1R segment 8	90 nts
SEQ ID NO: 1182	Polypeptide encoded by SEQ ID NO: 1181	30 aa
SEQ ID NO: 1183	MUC1R segment 9	90 nts
SEQ ID NO: 1184	Polypeptide encoded by SEQ ID NO: 1183	30 aa
SEQ ID NO: 1185	MUC1R segment 10	90 nts
SEQ ID NO: 1186	Polypeptide encoded by SEQ ID NO: 1185	30 aa
SEQ ID NO: 1187	MUC1R segment 11	90 nts
SEQ ID NO: 1188	Polypeptide encoded by SEQ ID NO: 1187	30 aa
SEQ ID NO: 1189	MUC1R segment 12	90 nts
SEQ ID NO: 1190	Polypeptide encoded by SEQ ID NO: 1189	30 aa
SEQ ID NO: 1191	MUC1R segment 13	90 nts
SEQ ID NO: 1192	Polypeptide encoded by SEQ ID NO: 1191	30 aa
SEQ ID NO: 1193	MUC1R segment 14	90 nts
SEQ ID NO: 1194	Polypeptide encoded by SEQ ID NO: 1193	30 aa
SEQ ID NO: 1195	MUC1R segment 15	90 nts
SEQ ID NO: 1196	Polypeptide encoded by SEQ ID NO: 1195	30 aa
SEQ ID NO: 1197	MUC1R segment 16	90 nts
SEQ ID NO: 1198	Polypeptide encoded by SEQ ID NO: 1197	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER	2.00	<u> </u>
SEQ ID NO: 1199	MUC1R segment 17	90 nts
SEQ ID NO: 1200	Polypeptide encoded by SEQ ID NO: 1199	30 aa
SEQ ID NO: 1201	MUC1R segment 18	90 nts
SEQ ID NO: 1202	Polypeptide encoded by SEQ ID NO: 1201	30 aa
SEQ ID NO: 1203	MUC1R segment 19	90 nts
SEQ ID NO: 1204	Polypeptide encoded by SEQ ID NO: 1203	30 aa
SEQ ID NO: 1205	MUC1R segment 20	90 nts
SEQ ID NO: 1206	Polypeptide encoded by SEQ ID NO: 1205	30 aa
SEQ ID NO: 1207	MUC1R segment 21	48 nts
SEQ ID NO: 1208	Polypeptide encoded by SEQ ID NO: 1207	16 aa
SEQ ID NO: 1209	Differentiation Savine	16638 nts
SEQ ID NO: 1210	Polypeptide encoded by SEQ ID NO: 1209	5546 aa
SEQ ID NO: 1211	BAGE segment 1	90 nts
SEQ ID NO: 1212	Polypeptide encoded by SEQ ID NO: 1211	30 aa
SEQ ID NO: 1213	BAGE segment 2	90 nts
SEQ ID NO: 1214	Polypeptide encoded by SEQ ID NO: 1213	30 aa
SEQ ID NO: 1215	BAGE segment 3	51 nts
SEQ ID NO: 1216	Polypeptide encoded by SEQ ID NO: 1215	17 aa
SEQ ID NO: 1217	GAGE-1 segment 1	90 nts
SEQ ID NO: 1218	Polypeptide encoded by SEQ ID NO: 1217	30 aa
SEQ ID NO: 1219	GAGE-1 segment 2	90 nts
SEQ ID NO: 1220	Polypeptide encoded by SEQ ID NO: 1219	30 aa
SEQ ID NO: 1221	GAGE-1 segment 3	90 nts
SEQ ID NO: 1222	Polypeptide encoded by SEQ ID NO: 1221	30 aa



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1223	GAGE-1 segment 4	90 nts
SEQ ID NO: 1224	Polypeptide encoded by SEQ ID NO: 1223	30 aa
SEQ ID NO: 1225	GAGE-1 segment 5	90 nts
SEQ ID NO: 1226	Polypeptide encoded by SEQ ID NO: 1225	30 aa
SEQ ID NO: 1227	GAGE-1 segment 6	90 nts
SEQ ID NO: 1228	Polypeptide encoded by SEQ ID NO: 1227	30 aa
SEQ ID NO: 1229	GAGE-1 segment 7	90 nts
SEQ ID NO: 1230	Polypeptide encoded by SEQ ID NO: 1229	30 aa
SEQ ID NO: 1231	GAGE-1 segment 8	90 nts
SEQ ID NO: 1232	Polypeptide encoded by SEQ ID NO: 1231	30 aa
SEQ ID NO: 1233	GAGE-1 segment 9	66 nts
SEQ ID NO: 1234	Polypeptide encoded by SEQ ID NO: 1233	22 aa
SEQ ID NO: 1235	gp100ln4 segment 1	90 nts
SEQ ID NO: 1236	Polypeptide encoded by SEQ ID NO: 1235	30 aa
SEQ ID NO: 1237	gp100ln4 segment 2	90 nts
SEQ ID NO: 1238	Polypeptide encoded by SEQ ID NO: 1237	30 aa
SEQ ID NO: 1239	gp100ln4 segment 3	75 nts
SEQ ID NO: 1240	Polypeptide encoded by SEQ ID NO: 1239	25 aa
SEQ ID NO: 1241	MAGE-1 segment 1	90 nts
SEQ ID NO: 1242	Polypeptide encoded by SEQ ID NO: 1241	30 aa
SEQ ID NO: 1243	MAGE-1 segment 2	90 nts
SEQ ID NO: 1244	Polypeptide encoded by SEQ ID NO: 1243	30 aa
SEQ ID NO: 1245	MAGE-1 segment 3	90 nts
SEQ ID NO: 1246	Polypeptide encoded by SEQ ID NO: 1245	30 aa

SEQUENCE ID MUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1247	MAGE-1 segment 4	90 nts
SEQ ID NO: 1248	Polypeptide encoded by SEQ ID NO: 1247	30 aa
SEQ ID NO: 1249	MAGE-1 segment 5	90 nts
SEQ ID NO: 1250	Polypeptide encoded by SEQ ID NO: 1249	30 aa
SEQ ID NO: 1251	MAGE-1 segment 6	90 nts
SEQ ID NO: 1252	Polypeptide encoded by SEQ ID NO: 1251	30 aa
SEQ ID NO: 1253	MAGE-1 segment 7	90 nts
SEQ ID NO: 1254	Polypeptide encoded by SEQ ID NO: 1253	30 aa
SEQ ID NO: 1255	MAGE-1 segment 8	90 nts
SEQ ID NO: 1256	Polypeptide encoded by SEQ ID NO: 1255	30 aa
SEQ ID NO: 1257	MAGE-1 segment 9	90 nts
SEQ ID NO: 1258	Polypeptide encoded by SEQ ID NO: 1257	30 aa
SEQ ID NO: 1259	MAGE-1 segment 10	90 nts
SEQ ID NO: 1260	Polypeptide encoded by SEQ ID NO: 1259	30 aa
SEQ ID NO: 1261	MAGE-1 segment 11	90 nts
SEQ ID NO: 1262	Polypeptide encoded by SEQ ID NO: 1261	30 aa
SEQ ID NO: 1263	MAGE-1 segment 12	90 nts
SEQ ID NO: 1264	Polypeptide encoded by SEQ ID NO: 1263	30 aa
SEQ ID NO: 1265	MAGE-1 segment 13	90 nts
SEQ ID NO: 1266	Polypeptide encoded by SEQ ID NO: 1265	30 aa
SEQ ID NO: 1267	MAGE-1 segment 14	90 nts
SEQ ID NO: 1268	Polypeptide encoded by SEQ ID NO: 1267	30 aa
SEQ ID NO: 1269	MAGE-1 segment 15	90 nts
SEQ ID NO: 1270	Polypeptide encoded by SEQ ID NO: 1269	30 aa

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SEQUIENCE ID NUMBER	SEQUENCE	ILENGTH
SEQ ID NO: 1271	MAGE-1 segment 16	90 nts
SEQ ID NO: 1272	Polypeptide encoded by SEQ ID NO: 1271	30 aa
SEQ ID NO: 1273	MAGE-1 segment 17	90 nts
SEQ ID NO: 1274	Polypeptide encoded by SEQ ID NO: 1273	30 aa
SEQ ID NO: 1275	MAGE-1 segment 18	90 nts
SEQ ID NO: 1276	Polypeptide encoded by SEQ ID NO: 1275	30 aa
SEQ ID NO: 1277	MAGE-1 segment 19	90 nts
SEQ ID NO: 1278	Polypeptide encoded by SEQ ID NO: 1277	30 aa
SEQ ID NO: 1279	MAGE-1 segment 20	84 nts
SEQ ID NO: 1280	Polypeptide encoded by SEQ ID NO: 1279	28 aa
SEQ ID NO: 1281	MAGE-3 segment 1	90 nts
SEQ ID NO: 1282	Polypeptide encoded by SEQ ID NO: 1281	30 aa .
SEQ ID NO: 1283	MAGE-3 segment 2	90 nts
SEQ ID NO: 1284	Polypeptide encoded by SEQ ID NO: 1283	30 aa
SEQ ID NO: 1285	MAGE-3 segment 3	90 nts
SEQ ID NO: 1286	Polypeptide encoded by SEQ ID NO: 1285	30 aa
SEQ ID NO: 1287	MAGE-3 segment 4	90 nts
SEQ ID NO: 1288	Polypeptide encoded by SEQ ID NO: 1287	30 aa
SEQ ID NO: 1289	MAGE-3 segment 5	90 nts
SEQ ID NO: 1290	Polypeptide encoded by SEQ ID NO: 1289	30 aa
SEQ ID NO: 1291	MAGE-3 segment 6	90 nts
SEQ ID NO: 1292	Polypeptide encoded by SEQ ID NO: 1291	30 aa
SEQ ID NO: 1293	MAGE-3 segment 7	90 nts
SEQ ID NO: 1294	Polypeptide encoded by SEQ ID NO: 1293	30 aa

SEQUENCE ID MUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1295	MAGE-3 segment 8	90 nts
SEQ ID NO: 1296	Polypeptide encoded by SEQ ID NO: 1295	30 aa
SEQ ID NO: 1297	MAGE-3 segment 9	90 nts
SEQ ID NO: 1298	Polypeptide encoded by SEQ ID NO: 1297	30 aa
SEQ ID NO: 1299	MAGE-3 segment 10	90 nts
SEQ ID NO: 1300	Polypeptide encoded by SEQ ID NO: 1299	30 aa
SEQ ID NO: 1301	MAGE-3 segment 11	90 nts
SEQ ID NO: 1302	Polypeptide encoded by SEQ ID NO: 1301	30 aa
SEQ ID NO: 1303	MAGE-3 segment 12	90 nts
SEQ ID NO: 1304	Polypeptide encoded by SEQ ID NO: 1303	30 aa
SEQ ID NO: 1305	MAGE-3 segment 13	90 nts
SEQ ID NO: 1306	Polypeptide encoded by SEQ ID NO: 1305	30 aa
SEQ ID NO: 1307	MAGE-3 segment 14	90 nts
SEQ ID NO: 1308	Polypeptide encoded by SEQ ID NO: 1307	30 aa
SEQ ID NO: 1309	MAGE-3 segment 15	90 nts
SEQ ID NO: 1310	Polypeptide encoded by SEQ ID NO: 1309	30 aa
SEQ ID NO: 1311	MAGE-3 segment 16	90 nts
SEQ ID NO: 1312	Polypeptide encoded by SEQ ID NO: 1311	30 aa
SEQ ID NO: 1313	MAGE-3 segment 17	90 nts
SEQ ID NO: 1314	Polypeptide encoded by SEQ ID NO: 1313	30 aa
SEQ ID NO: 1315	MAGE-3 segment 18	90 nts
SEQ ID NO: 1316	Polypeptide encoded by SEQ ID NO: 1315	30 aa
SEQ ID NO: 1317	MAGE-3 segment 19	90 nts
SEQ ID NO: 1318	Polypeptide encoded by SEQ ID NO: 1317	30 aa



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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1319	MAGE-3 segment 20	90 nts
SEQ ID NO: 1320	Polypeptide encoded by SEQ ID NO: 1319	30 aa
SEQ ID NO: 1321	MAGE-3 segment 21	54 nts
SEQ ID NO: 1322	Polypeptide encoded by SEQ ID NO: 1321	18 aa
SEQ ID NO: 1323	PRAME segment 1	90 nts
SEQ ID NO: 1324	Polypeptide encoded by SEQ ID NO: 1323	30 aa
SEQ ID NO: 1325	PRAME segment 2	90 nts
SEQ ID NO: 1326	Polypeptide encoded by SEQ ID NO: 1325	30 aa
SEQ ID NO: 1327	PRAME segment 3	90 nts
SEQ ID NO: 1328	Polypeptide encoded by SEQ ID NO: 1327	30 aa
SEQ ID NO: 1329	PRAME segment 4 -	90 nts
SEQ ID NO: 1330	Polypeptide encoded by SEQ ID NO: 1329	30 aa
SEQ ID NO: 1331	PRAME segment 5	90 nts
SEQ ID NO: 1332	Polypeptide encoded by SEQ ID NO: 1331	30 aa
SEQ ID NO: 1333	PRAME segment 6	90 nts
SEQ ID NO: 1334	Polypeptide encoded by SEQ ID NO: 1333	30 aa
SEQ ID NO: 1335	PRAME segment 7	90 nts
SEQ ID NO: 1336	Polypeptide encoded by SEQ ID NO: 1335	30 aa
SEQ ID NO: 1337	PRAME segment 8	90 nts
SEQ ID NO: 1338	Polypeptide encoded by SEQ ID NO: 1337	30 aa
SEQ ID NO: 1339	PRAME segment 9	90 nts
SEQ ID NO: 1340	Polypeptide encoded by SEQ ID NO: 1339	30 aa
SEQ ID NO: 1341	PRAME segment 10	90 nts
SEQ ID NO: 1342	Polypeptide encoded by SEQ ID NO: 1341	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1343	PRAME segment 11	90 nts
SEQ ID NO: 1344	Polypeptide encoded by SEQ ID NO: 1343	30 aa
SEQ ID NO: 1345	PRAME segment 12	90 nts
SEQ ID NO: 1346	Polypeptide encoded by SEQ ID NO: 1345	30 aa
SEQ ID NO: 1347	PRAME segment 13	90 nts
SEQ ID NO: 1348	Polypeptide encoded by SEQ ID NO: 1347	30 aa
SEQ ID NO: 1349	PRAME segment 14	90 nts
SEQ ID NO: 1350	Polypeptide encoded by SEQ ID NO: 1349	30 aa
SEQ ID NO: 1351	PRAME segment 15	90 nts
SEQ ID NO: 1352	Polypeptide encoded by SEQ ID NO: 1351	30 aa
SEQ ID NO: 1353	PRAME segment 16.	90 nts
SEQ ID NO: 1354	Polypeptide encoded by SEQ ID NO: 1353	30 aa
SEQ ID NO: 1355	PRAME segment 17	90 nts
SEQ ID NO: 1356	Polypeptide encoded by SEQ ID NO: 1355	30 aa
SEQ ID NO: 1357	PRAME segment 18	90 nts
SEQ ID NO: 1358	Polypeptide encoded by SEQ ID NO: 1357	30 aa
SEQ ID NO: 1359	PRAME segment 19	90 nts
SEQ ID NO: 1360	Polypeptide encoded by SEQ ID NO: 1359	30 aa
SEQ ID NO: 1361	PRAME segment 20	90 nts
SEQ ID NO: 1362	Polypeptide encoded by SEQ ID NO: 1361	30 aa
SEQ ID NO: 1363	PRAME segment 21	90 nts
SEQ ID NO: 1364	Polypeptide encoded by SEQ ID NO: 1363	30 aa
SEQ ID NO: 1365	PRAME segment 22	90 nts
SEQ ID NO: 1366	Polypeptide encoded by SEQ ID NO: 1365	30 aa



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SEQUENCE ID	SEQUENCE	ILENGTH
NUMBER		
SEQ ID NO: 1367	PRAME segment 23	90 nts
SEQ ID NO: 1368	Polypeptide encoded by SEQ ID NO: 1367	30 aa
SEQ ID NO: 1369	PRAME segment 24	90 nts
SEQ ID NO: 1370	Polypeptide encoded by SEQ ID NO: 1369	30 aa
SEQ ID NO: 1371	PRAME segment 25	90 nts
SEQ ID NO: 1372	Polypeptide encoded by SEQ ID NO: 1371	30 aa
SEQ ID NO: 1373	PRAME segment 26	90 nts
SEQ ID NO: 1374	Polypeptide encoded by SEQ ID NO: 1373	30 aa
SEQ ID NO: 1375	PRAME segment 27	90 nts
SEQ ID NO: 1376	Polypeptide encoded by SEQ ID NO: 1375	30 aa
SEQ ID NO: 1377	PRAME segment 28	90 nts
SEQ ID NO: 1378	Polypeptide encoded by SEQ ID NO: 1377	30 aa
SEQ ID NO: 1379	PRAME segment 29	90 nts
SEQ ID NO: 1380	Polypeptide encoded by SEQ ID NO: 1379	30 aa
SEQ ID NO: 1381	PRAME segment 30	90 nts
SEQ ID NO: 1382	Polypeptide encoded by SEQ ID NO: 1381	30 aa
SEQ ID NO: 1383	PRAME segment 31	90 nts
SEQ ID NO: 1384	Polypeptide encoded by SEQ ID NO: 1383	30 aa
SEQ ID NO: 1385	PRAME segment 32	90 nts
SEQ ID NO: 1386	Polypeptide encoded by SEQ ID NO: 1385	30 aa
SEQ ID NO: 1387	PRAME segment 33	90 nts
SEQ ID NO: 1388	Polypeptide encoded by SEQ ID NO: 1387	30 aa
SEQ ID NO: 1389	PRAME segment 34	54 nts
SEQ ID NO: 1390	Polypeptide encoded by SEQ ID NO: 1389	18 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1391	TRP2IN2 segment 1	90 nts
SEQ ID NO: 1392	Polypeptide encoded by SEQ ID NO: 1391	30 aa
SEQ ID NO: 1393	TRP2IN2 segment 2	90 nts
SEQ ID NO: 1394	Polypeptide encoded by SEQ ID NO: 1393	30 aa
SEQ ID NO: 1395	TRP2IN2 segment 3	84 nts
SEQ ID NO: 1396	Polypeptide encoded by SEQ ID NO: 1395	28 aa
SEQ ID NO: 1397	NYNSO1a segment 1	90 nts
SEQ ID NO: 1398	Polypeptide encoded by SEQ ID NO: 1397	30 aa
SEQ ID NO: 1399	NYNSO1a segment 2	90 nts
SEQ ID NO: 1400	Polypeptide encoded by SEQ ID NO: 1399	30 aa
SEQ ID NO: 1401	NYNSO1a segment 3	90 nts
SEQ ID NO: 1402	Polypeptide encoded by SEQ ID NO: 1401	30 aa
SEQ ID NO: 1403	NYNSO1a segment 4	90 nts
SEQ ID NO: 1404	Polypeptide encoded by SEQ ID NO: 1403	30 aa
SEQ ID NO: 1405	NYNSO1a segment 5	90 nts
SEQ ID NO: 1406	Polypeptide encoded by SEQ ID NO: 1405	30 aa
SEQ ID NO: 1407	NYNSO1a segment 6	90 nts
SEQ ID NO: 1408	Polypeptide encoded by SEQ ID NO: 1407	30 aa
SEQ ID NO: 1409	NYNSO1a segment 7	90 nts
SEQ ID NO: 1410	Polypeptide encoded by SEQ ID NO: 1409	30 aa
SEQ ID NO: 1411	NYNSO1a segment 8	90 nts
SEQ ID NO: 1412	Polypeptide encoded by SEQ ID NO: 1411	30 aa
SEQ ID NO: 1413	NYNSO1a segment 9	90 nts
SEQ ID NO: 1414	Polypeptide encoded by SEQ ID NO: 1413	30 aa



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SEQUENCE IID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1415	NYNSO1a segment 10	90 nts
SEQ ID NO: 1416	Polypeptide encoded by SEQ ID NO: 1415	30 aa
SEQ ID NO: 1417	NYNSO1a segment 11	90 nts
SEQ ID NO: 1418	Polypeptide encoded by SEQ ID NO: 1417	30 aa
SEQ ID NO: 1419	NYNSO1a segment 12	57 nts ,
SEQ ID NO: 1420	Polypeptide encoded by SEQ ID NO: 1419	19 aa
SEQ ID NO: 1421	NYNSO1b segment 1	90 nts
SEQ ID NO: 1422	Polypeptide encoded by SEQ ID NO: 1421	30 aa
SEQ ID NO: 1423	NYNSO1b segment 2	90 nts
SEQ ID NO: 1424	Polypeptide encoded by SEQ ID NO: 1423	30 aa
SEQ ID NO: 1425	NYNSO1b segment 3	90 nts
SEQ ID NO: 1426	Polypeptide encoded by SEQ ID NO: 1425	30 aa .
SEQ ID NO: 1427	NYNSO1b segment 4	51 nts
SEQ ID NO: 1428	Polypeptide encoded by SEQ ID NO: 1427	
SEQ ID NO: 1429	LAGE1 segment 1	90 nts
SEQ ID NO: 1430	Polypeptide encoded by SEQ ID NO: 1429	30 aa
SEQ ID NO: 1431	LAGE1 segment 2	90 nts
SEQ ID NO: 1432	Polypeptide encoded by SEQ ID NO: 1431	30 aa
SEQ ID NO: 1433	LAGE1 segment 3	90 nts
SEQ ID NO: 1434	Polypeptide encoded by SEQ ID NO: 1433	30 aa
SEQ ID NO: 1435	LAGE1 segment 4	90 nts
SEQ ID NO: 1436	Polypeptide encoded by SEQ ID NO: 1435	30 aa
SEQ ID NO: 1437	LAGE1 segment 5	90 nts
SEQ ID NO: 1438	Polypeptide encoded by SEQ ID NO: 1437	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1439	LAGE1 segment 6	90 nts
SEQ ID NO: 1440	Polypeptide encoded by SEQ ID NO: 1439	30 aa
SEQ ID NO: 1441	LAGE1 segment 7	90 nts
SEQ ID NO: 1442	Polypeptide encoded by SEQ ID NO: 1441	30 aa
SEQ ID NO: 1443	LAGE1 segment 8	90 nts
SEQ ID NO: 1444	Polypeptide encoded by SEQ ID NO: 1443	30 aa
SEQ ID NO: 1445	LAGE1 segment 9	90 nts
SEQ ID NO: 1446	Polypeptide encoded by SEQ ID NO: 1445	30 aa
SEQ ID NO: 1447	LAGE1 segment 10	90 nts
SEQ ID NO: 1448	Polypeptide encoded by SEQ ID NO: 1447	30 aa
SEQ ID NO: 1449	LAGE1 segment 11	90 nts
SEQ ID NO: 1450	Polypeptide encoded by SEQ ID NO: 1449	30 aa
SEQ ID NO: 1451	LAGE1 segment 12	57 nts
SEQ ID NO: 1452	Polypeptide encoded by SEQ ID NO: 1451	19 aa
SEQ ID NO: 1453	Melanoma cancer specific Savine	10623 nts
SEQ ID NO: 1454	Polypeptide encoded by SEQ ID NO: 1453	3541 aa
SEQ ID NO: 1455	Figure 16 A1S1 99mer	99 nts
SEQ ID NO: 1456	Figure 16 A1S2 100mer	100 nts
SEQ ID NO: 1457	Figure 16 A1S3 100mer	100 nts
SEQ ID NO: 1458	Figure 16 A1S4 100mer	100 nts
SEQ ID NO: 1459	Figure 16 A1S5 100mer	100 nts
SEQ ID NO: 1460	Figure 16 A1S6 99mer	99 nts
SEQ ID NO: 1461	Figure 16 A1S7 97mer	99 nts
SEQ ID NO: 1462	Figure 16 A1S8 100mer	100 nts



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SEQUIENCE IID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1463	Figure 16 A1S9 100mer	100 nts
SEQ ID NO: 1464	Figure 16 A1S10 75mer	76 nts
SEQ ID NO: 1465	Figure 16 A1F 20mer	20 nts
SEQ ID NO: 1466	Figure 16 A1R 20mer	20 nts
SEQ ID NO: 1467	Amino acid sequence of immunostimulatory domain of an invasin protein from Yersinia spp.	16 aa

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DETAILED DESCRIPTION OF THE INVENTION

1. Definitions

The articles "a" and "an" are used herein to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

As used herein, the term "about" refers to a quantity, level, value, dimension, size, or amount that varies by as much as 30%, preferably by as much as 20%, and more preferably by as much as 10% to a reference quantity, level, value, dimension, size, or amount.

By "antigen-binding molecule" is meant a molecule that has binding affinity for a target antigen. It will be understood that this term extends to immunoglobulins, immunoglobulin fragments and non-immunoglobulin derived protein frameworks that exhibit antigen-binding activity.

The term "clade" as used herein refers to a hypothetical species of an organism and its descendants or a monophyletic group of organisms. Clades carry a definition, based on ancestry, and a diagnosis, based on synapomorphies. It should be noted that diagnoses of clades could change while definitions do not.

Throughout this specification, unless the context requires otherwise, the words "comprise", "comprises" and "comprising" will be understood to imply the inclusion of a stated step or element or group of steps or elements but not the exclusion of any other step or element or group of steps or elements.

By "expression vector" is meant any autonomous genetic element capable of directing the synthesis of a protein encoded by the vector. Such expression vectors are known by practitioners in the art.

As used herein, the term "function" refers to a biological, enzymatic, or therapeutic function.

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"Homology" refers to the percentage number of amino acids that are identical or constitute conservative substitutions as defined in Table B infra. Homology may be determined using sequence comparison programs such as GAP (Deveraux et al. 1984, Nucleic Acids Research 12, 387-395). In this way, sequences of a similar or substantially different length to those cited herein might be compared by insertion of gaps into the alignment, such gaps being determined, for example, by the comparison algorithm used by GAP.

To enhance an immune response ("immunoenhancement"), as is well-known in the art, means to increase an animal's capacity to respond to foreign or disease-specific antigens (e.g., cancer antigens) i.e., those cells primed to attack such antigens are increased in number, activity, and ability to detect and destroy the those antigens. Strength of immune response is measured by standard tests including: direct measurement of peripheral blood lymphocytes by means known to the art; natural killer cell cytotoxicity assays (see, e.g., Provinciali M. et al (1992, J. Immunol. Meth. 155: 19-24), cell proliferation assays (see, e.g., Vollenweider, I. and Groseurth, P. J. (1992, J. Immunol. Meth. 149: 133-135), immunoassays of immune cells and subsets (see, e.g., Loeffler, D. A., et al. (1992, Cytom. 13: 169-174); Rivoltini, L., et al. (1992, Can. Immunol. Immunother, 34: 241-251); or skin tests for cell-mediated immunity (see, e.g., Chang, A. E. et al (1993, Cancer Res. 53: 1043-1050). Any statistically significant increase in strength of immune response as measured by the foregoing tests is considered "enhanced immune response" "immunoenhancement" or "immunopotentiation" as used herein. Enhanced immune response is also indicated by physical manifestations such as fever and inflammation, as well as healing of systemic and local infections, and reduction of symptoms in disease, i.e., decrease in tumour size, alleviation of symptoms of a disease or condition including, but not restricted to, leprosy, tuberculosis, malaria, naphthous ulcers, herpetic and papillomatous warts, gingivitis, artherosclerosis, the concomitants of AIDS such as Kaposi's sarcoma, bronchial infections, and the like. Such physical manifestations response" "immunoenhancement" "enhanced or also define immune "immunopotentiation" as used herein.

Reference herein to "immuno-interactive" includes reference to any interaction, reaction, or other form of association between molecules and in particular where one of the molecules is, or mimics, a component of the immune system.

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By "isolated" is meant material that is substantially or essentially free from components that normally accompany it in its native state.

By "modulating" is meant increasing or decreasing, either directly or indirectly, an immune response against a target antigen of a member selected from the group consisting of a cancer and an organism, preferably a pathogenic organism.

By "natural gene" is meant a gene that naturally encodes a protein.

The term "natural polypeptide" as used herein refers to a polypeptide that exists in nature.

By "obtained from" is meant that a sample such as, for example, a polynucleotide extract or polypeptide extract is isolated from, or derived from, a particular source of the host. For example, the extract can be obtained from a tissue or a biological fluid isolated directly from the host.

The term "oligonucleotide" as used herein refers to a polymer composed of a multiplicity of nucleotide residues (deoxyribonucleotides or ribonucleotides, or related structural variants or synthetic analogues thereof) linked via phosphodiester bonds (or related structural variants or synthetic analogues thereof). Thus, while the term "oligonucleotide" typically refers to a nucleotide polymer in which the nucleotide residues and linkages between them are naturally occurring, it will be understood that the term also includes within its scope various analogues including, but not restricted to, peptide nucleic acids (PNAs), phosphoramidates, phosphorothioates, methyl phosphonates, 2-O-methyl ribonucleic acids, and the like. The exact size of the molecule can vary depending on the particular application. An oligonucleotide is typically rather short in length, generally from about 10 to 30 nucleotide residues, but the term can refer to molecules of any length, although the term "polynucleotide" or "nucleic acid" is typically used for large oligonucleotides.

By "operably linked" is meant that transcriptional and translational regulatory polynucleotides are positioned relative to a polypeptide-encoding polynucleotide in such a manner that the polynucleotide is transcribed and the polypeptide is translated.

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The term "parent polypeptide" as used herein typically refers to a polypeptide encoded by a natural gene. However, it is possible that the parent polypeptide corresponds to a protein that is not naturally-occurring but has been engineered using recombinant techniques. In this instance, a polynucleotide encoding the parent polypeptide may comprise different but synonymous codons relative to a natural gene encoding the same polypeptide. Alternatively, the parent polypeptide may not correspond to a natural polypeptide sequence. For example, the parent polypeptide may comprise one or more consensus sequences common to a plurality of polypeptides.

The term "patient" refers to patients of human or other mammal and includes any individual it is desired to examine or treat using the methods of the invention. However, it will be understood that "patient" does not imply that symptoms are present. Suitable mammals that fall within the scope of the invention include, but are not restricted to, primates, livestock animals (e.g., sheep, cows, horses, donkeys, pigs), laboratory test animals (e.g., rabbits, mice, rats, guinea pigs, hamsters), companion animals (e.g., cats, dogs) and captive wild animals (e.g., foxes, deer, dingoes).

By "pharmaceutically-acceptable carrier" is meant a solid or liquid filler, diluent or encapsulating substance that can be safely used in topical or systemic administration to a mammal.

"Polypeptide", "peptide" and "protein" are used interchangeably herein to refer to a polymer of amino acid residues and to variants and synthetic analogues of the same. Thus, these terms apply to amino acid polymers in which one or more amino acid residues is a synthetic non-naturally occurring amino acid, such as a chemical analogue of a corresponding naturally occurring amino acid, as well as to naturally-occurring amino acid polymers.

The term "polynucleotide" or "nucleic acid" as used herein designates mRNA, RNA, cRNA, cDNA or DNA. The term typically refers to oligonucleotides greater than 30 nucleotide residues in length.

By "primer" is meant an oligonucleotide which, when paired with a strand of DNA, is capable of initiating the synthesis of a primer extension product in the presence of a suitable polymerising agent. The primer is preferably single-stranded for maximum

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efficiency in amplification but can alternatively be double-stranded. A primer must be sufficiently long to prime the synthesis of extension products in the presence of the polymerisation agent. The length of the primer depends on many factors, including application, temperature to be employed, template reaction conditions, other reagents, and source of primers. For example, depending on the complexity of the target sequence, the oligonucleotide primer typically contains 15 to 35 or more nucleotide residues, although it can contain fewer nucleotide residues. Primers can be large polynucleotides, such as from about 35 nucleotides to several kilobases or more. Primers can be selected to be "substantially complementary" to the sequence on the template to which it is designed to hybridise and serve as a site for the initiation of synthesis. By "substantially complementary", it is meant that the primer is sufficiently complementary to hybridise with a target polynucleotide. Preferably, the primer contains no mismatches with the template to which it is designed to hybridise but this is not essential. For example, noncomplementary nucleotide residues can be attached to the 5' end of the primer, with the remainder of the primer sequence being complementary to the template. Alternatively, non-complementary nucleotide residues or a stretch of non-complementary nucleotide residues can be interspersed into a primer, provided that the primer sequence has sufficient complementarity with the sequence of the template to hybridise therewith and thereby form a template for synthesis of the extension product of the primer.

"Probe" refers to a molecule that binds to a specific sequence or sub-sequence or other moiety of another molecule. Unless otherwise indicated, the term "probe" typically refers to a polynucleotide probe that binds to another polynucleotide, often called the "target polynucleotide", through complementary base pairing. Probes can bind target polynucleotides lacking complete sequence complementarity with the probe, depending on the stringency of the hybridisation conditions. Probes can be labelled directly or indirectly.

By "recombinant polypeptide" is meant a polypeptide made using recombinant techniques, i.e., through the expression of a recombinant or synthetic polynucleotide.

Terms used to describe sequence relationships between two or more polynucleotides or polypeptides include "reference sequence", "comparison window", "sequence identity", "percentage of sequence identity" and "substantial identity". A "reference sequence" is at least 12 but frequently 15 to 18 and often at least 25 monomer

units, inclusive of nucleotides and amino acid residues, in length. Because two polynucleotides may each comprise (1) a sequence (i.e., only a portion of the complete polynucleotide sequence) that is similar between the two polynucleotides, and (2) a sequence that is divergent between the two polynucleotides, sequence comparisons between two (or more) polynucleotides are typically performed by comparing sequences of the two polynucleotides over a "comparison window" to identify and compare local regions of sequence similarity. A "comparison window" refers to a conceptual segment of at least 50 contiguous positions, usually about 50 to about 100, more usually about 100 to about 150 in which a sequence is compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. The comparison window may comprise additions or deletions (i.e., gaps) of about 20% or less as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. Optimal alignment of sequences for aligning a comparison window may be conducted by computerised implementations of algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Drive Madison, WI, USA) or by inspection and the best alignment (i.e., resulting in the highest percentage homology over the comparison window) generated by any of the various methods selected. Reference also may be made to the BLAST family of programs as for example disclosed by Altschul et al., 1997, Nucl. Acids Res. 25:3389. A detailed discussion of sequence analysis can be found in Unit 19.3 of Ausubel et al., "Current Protocols in Molecular Biology", John Wiley & Sons Inc, 1994-1998, Chapter 15.

The term "sequence identity" as used herein refers to the extent that sequences are identical on a nucleotide-by-nucleotide basis or an amino acid-by-amino acid basis over a window of comparison. Thus, a "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over the window of comparison, determining the number of positions at which the identical nucleic acid base (e.g., A, T, C, G, I) or the identical amino acid residue (e.g., Ala, Pro, Ser, Thr, Gly, Val, Leu, Ile, Phe, Tyr, Trp, Lys, Arg, His, Asp, Glu, Asn, Gln, Cys and Met) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison (i.e., the window size), and multiplying the result by 100 to yield the percentage of sequence identity. For the purposes of the present

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invention, "sequence identity" will be understood to mean the "match percentage" calculated by the DNASIS computer program (Version 2.5 for windows; available from Hitachi Software engineering Co., Ltd., South San Francisco, California, USA) using standard defaults as used in the reference manual accompanying the software.

The term "synthetic polynucleotide" as used herein refers to a polynucleotide formed in vitro by the manipulation of a polynucleotide into a form not normally found in nature. For example, the synthetic polynucleotide can be in the form of an expression vector. Generally, such expression vectors include transcriptional and translational regulatory polynucleotide operably linked to the polynucleotide.

The term "synonymous codon" as used herein refers to a codon having a different nucleotide sequence than another codon but encoding the same amino acid as that other codon.

By "translational efficiency" is meant the efficiency of a cell's protein synthesis machinery to incorporate the amino acid encoded by a codon into a nascent polypeptide chain. This efficiency can be evidenced, for example, by the rate at which the cell is able to synthesise the polypeptide from an RNA template comprising the codon, or by the amount of the polypeptide synthesised from such a template.

By "vector" is meant a polynucleotide molecule, preferably a DNA molecule derived, for example, from a plasmid, bacteriophage, yeast or virus, into which a polynucleotide can be inserted or cloned. A vector preferably contains one or more unique restriction sites and can be capable of autonomous replication in a defined host cell including a target cell or tissue or a progenitor cell or tissue thereof, or be integrable with the genome of the defined host such that the cloned sequence is reproducible. Accordingly, the vector can be an autonomously replicating vector, i.e., a vector that exists as an extrachromosomal entity, the replication of which is independent of chromosomal replication, e.g., a linear or closed circular plasmid, an extrachromosomal element, a minichromosome, or an artificial chromosome. The vector can contain any means for assuring self-replication. Alternatively, the vector can be one which, when introduced into the host cell, is integrated into the genome and replicated together with the chromosome(s) into which it has been integrated. A vector system can comprise a single vector or plasmid, two or more vectors or plasmids, which together contain the total DNA to be introduced

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into the genome of the host cell, or a transposon. The choice of the vector will typically depend on the compatibility of the vector with the host cell into which the vector is to be introduced. In the present case, the vector is preferably a viral or viral-derived vector, which is operably functional in animal and preferably mammalian cells. Such vector may be derived from a poxvirus, an adenovirus or yeast. The vector can also include a selection marker such as an antibiotic resistance gene that can be used for selection of suitable transformants. Examples of such resistance genes are known to those of skill in the art and include the *nptII* gene that confers resistance to the antibiotics kanamycin and G418 (Geneticin®) and the *hph* gene which confers resistance to the antibiotic hygromycin B.

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2. Synthetic polypeptides

The inventors have surprisingly discovered that the structure of a parent polypeptide can be disrupted sufficiently to impede, abrogate or otherwise alter at least one function of the parent polypeptide, while simultaneously minimising the destruction of potentially useful epitopes that are present in the parent polypeptide, by fusing, coupling or otherwise linking together different segments of the parent polypeptide in a different relationship relative to their linkage in the parent polypeptide. As a result of this change in relationship, the sequence of the linked segments in the resulting synthetic polypeptide is different to a sequence contained within the parent polypeptide. The synthetic polypeptides of the invention are useful as immunopotentiating agents, and are referred to elsewhere in the specification as scrambled antigen vaccines, super attenuated vaccines or "Savines".

Thus, the invention broadly resides in a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein said segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

It is preferable but not essential that the segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to that of corresponding segments in said at least one parent polypeptide. For example, in the case of a parent polypeptide that comprises three contiguous or overlapping segments A-B-C-D, these segments may be linked in 23 other possible orders to form a synthetic polypeptide. These orders may be selected from the group consisting of: A-B-D-C, A-C-B-D, A-C-D-B, A-D-B-C, A-D-C-B, B-A-C-D, B-A-D-C, B-C-A-D, B-C-D-A, B-D-A-C, B-D-C-A, C-A-B-D, C-A-D-B, C-B-A-D, C-B-D-A, C-D-B-A, D-A-B-C, D-A-C-B, D-B-A-C, D-B-C-A, D-C-A-B, and D-C-B-A. Although the rearrangement of the segments is preferably random, it is especially preferable to exclude or otherwise minimise rearrangements that result in complete or partial reassembly of the parent sequence (e.g., ADBC, BACD, DABC). It will be appreciated, however, that the probability of such complete or partial reassembly diminishes as the number of segments for rearrangement increases.

The order of the segments is suitably shuffled, reordered or otherwise rearranged relative to the order in which they exist in the parent polypeptide so that the structure of the polypeptide is disrupted sufficiently to impede, abrogate or otherwise alter at least one

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function associated with the parent polypeptide. Preferably, the segments of the parent polypeptide are randomly rearranged in the synthetic polypeptide.

The parent polypeptide is suitably a polypeptide that is associated with a disease or condition. For example, the parent polypeptide may be a polypeptide expressed by a pathogenic organism or a cancer. Alternatively, the parent polypeptide can be a self peptide related to an autoimmune disease including, but are not limited to, diseases such as diabetes (e.g., juvenile diabetes), multiple sclerosis, rheumatoid arthritis, myasthenia gravis, atopic dermatitis, and psoriasis and ankylosing spondylitis. Accordingly, the synthetic molecules of the present invention may also have utility for the induction of tolerance in a subject afflicted with an autoimmune disease or condition or with an allergy or other condition to which tolerance is desired. For example tolerance may be induced by contacting an immature dendritic cell of the individual to be treated with a synthetic polypeptide of the invention or by expressing in an immature dendritic cell a synthetic polynucleotide of the invention. Tolerance may also be induced against antigens causing allergic responses (e.g., asthma, hay fever). In this case, the parent polypeptide is suitably an allergenic protein including, but not restricted to, house-dust-mite allergenic proteins as for example described by Thomas and Smith (1998, Allergy, 53(9): 821-832).

The pathogenic organism includes, but is not restricted to, yeast, a virus, a bacterium, and a parasite. Any natural host of the pathogenic organism is contemplated by the present invention and includes, but is not limited to, mammals, avians and fish. In a preferred embodiment, the pathogenic organism is a virus, which may be an RNA virus or a DNA virus. Preferably, the RNA virus is Human Immunodeficiency Virus (HIV), Poliovirus, and Influenza virus, Rous sarcoma virus, or a Flavivirus such as Japanese encephalitis virus. In a preferred embodiment, the RNA virus is a Hepatitis virus including, but not limited to, Hepatitis strains A, B and C. Suitably, the DNA virus is a Herpesvirus including, but not limited to, Herpes simplex virus, Epstein-Barr virus, Cytomegalovirus and Parvovirus. In a preferred embodiment, the virus is HIV and the parent polypeptide is suitably selected from env, gag, pol, vif, vpr, tat, rev, vpu and nef, or combination thereof. In an alternate preferred embodiment, the virus is Hepatitis Cla virus and the parent polypeptide is the Hepatitis Cla virus polyprotein.

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In another embodiment, the pathogenic organism is a bacterium, which includes, but is not restricted to, Neisseria species, Meningococcal species, Haemophilus species Salmonella species, Streptococcal species, Legionella species and Mycobacterium species.

In yet another embodiment, the pathogenic organism is a parasite, which includes, but is not restricted to, *Plasmodium* species, *Schistosoma* species, *Leishmania* species, *Trypanosoma* species, *Toxoplasma* species and *Giardia* species.

Any cancer or tumour is contemplated by the present invention. For example, the cancer or tumour includes, but is not restricted to, melanoma, lung cancer, breast cancer, cervical cancer, prostate cancer, colon cancer, pancreatic cancer, stomach cancer, bladder cancer, kidney cancer, post transplant lymphoproliferative disease (PTLD), Hodgkin's Lymphoma and the like. Preferably, the cancer or tumour relates to melanoma. In a preferred embodiment of this type, the parent polypeptide is a melanocyte differentiation antigen which is suitably selected from gp100, MART, TRP-1, Tyros, TRP2, MC1R, MUC1F, MUC1R or a combination thereof. In an alternate preferred embodiment of this type, the parent polypeptide is a melanoma-specific antigen which is suitably selected from BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b, LAGE1 or a combination thereof.

In a preferred embodiment, the segments are selected on the basis of size. A segment according to the invention may be of any suitable size that can be utilised to elicit an immune response against an antigen encoded by the parent polypeptide. A number of factors can influence the choice of segment size. For example, the size of a segment should be preferably chosen such that it includes, or corresponds to the size of, T cell epitopes and their processing requirement. Practitioners in the art will recognise that class I-restricted T cell epitopes can be between 8 and 10 amino acids in length and if placed next to unnatural flanking residues, such epitopes can generally require 2 to 3 natural flanking amino acids to ensure that they are efficiently processed and presented. Class II-restricted T cell epitopes can range between 12 and 25 amino acids in length and may not require natural flanking residues for efficient proteolytic processing although it is believed that natural flanking residues may play a role. Another important feature of class II-restricted epitopes is that they generally contain a core of 9-10 amino acids in the middle which bind specifically to class II MHC molecules with flanking sequences either side of this core

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stabilising binding by associating with conserved structures on either side of class II MHC antigens in a sequence independent manner (Brown et al., 1993). Thus the functional region of class II-restricted epitopes is typically less than 15 amino acids long. The size of linear B cell epitopes and the factors effecting their processing, like class II-restricted epitopes, are quite variable although such epitopes are frequently smaller in size than 15 amino acids. From the foregoing, it is preferable, but not essential, that the size of the segment is at least 4 amino acids, preferably at least 7 amino acids, more preferably at least 12 amino acids, more preferably at least 20 amino acids and more preferably at least 30 amino acids. Suitably, the size of the segment is less than 2000 amino acids, more preferably less than 1000 amino acids, more preferably less than 500 amino acids, more preferably less than 200 amino acids, more preferably less than 100 amino acids, more preferably less than 80 amino acids and even more preferably less than 60 amino acids and still even more preferably less than 40 amino acids. In this regard, it is preferable that the size of the segments is as small as possible so that the synthetic polypeptide adopts a functionally different structure relative to the structure of the parent polypeptide. It is also preferable that the size of the segments is large enough to minimise loss of T cell epitopes. In an especially preferred embodiment, the size of the segment is about 30 amino acids.

An optional spacer may be utilised to space adjacent segments relative to each other. Accordingly, an optional spacer may be interposed between some or all of the segments. The spacer suitably alters proteolytic processing and/or presentation of adjacent segment(s). In a preferred embodiment of this type, the spacer promotes or otherwise enhances proteolytic processing and/or presentation of adjacent segment(s). Preferably, the spacer comprises at least one amino acid. The at least one amino acid is suitably a neutral amino acid. The neutral amino acid is preferably alanine. Alternatively, the at least one amino acid is cysteine.

In a preferred embodiment, segments are selected such that they have partial sequence identity or homology with one or more other segments. Suitably, at one or both ends of a respective segment there is comprised at least 4 contiguous amino acids, preferably at least 7 contiguous amino acids, more preferably at least 10 contiguous amino acids, more preferably at least 15 contiguous amino acids and even more preferably at least 20 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments. Preferably, at the or each

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end of a respective segment there is comprised less than 500 contiguous amino acids, more preferably less than 200 contiguous amino acids, more preferably less than 100 contiguous amino acids, more preferably less than 50 contiguous amino acids, more preferably less than 40 contiguous amino acids, and even more preferably less than 30 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments. Such sequence overlap (also referred to elsewhere in the specification as "overlapping fragments" or "overlapping segments") is preferable to ensure potential epitopes at segment boundaries are not lost and to ensure that epitopes at or near segment boundaries are processed efficiently if placed beside or near amino acids that inhibit processing. Preferably, the segment size is about twice the size of the overlap.

In a preferred embodiment, when segments have partial sequence homology therebetween, the homologous sequences suitably comprise conserved and/or non-conserved amino acid differences. Exemplary conservative substitutions are listed in the following table.

15 TABLE B

Original Residue	Examplary Substitutions
Ala	Ser
Arg	Lys
Asn	Gln, His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Рто
His	Asn, Gln
Ile	Leu, Val
Leu	Ile, Val

Original Residue	Exemplory Substitutions
Lys	Arg, Gln, Glu
Met	Leu, Ile,
Phe	Met, Leu, Tyr
Ser	Thr
Thr	Ser
Ттр	Туг
Туг	Trp, Phe
Val	Ile, Leu

Conserved or non-conserved differences may correspond to polymorphisms in corresponding parent polypeptides. Polymorphic polypeptides are expressed by various pathogenic organisms and cancers. For example, the polymorphic polypeptides may be expressed by different viral strains or clades or by cancers in different individuals.

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Sequence overlap between respective segments is preferable to minimise destruction of any epitope sequences that may result from any shuffling or rearrangement of the segments relative to their existing order in the parent polypeptide. If overlapping segments as described above are employed to form a synthetic polypeptide, it may not be 10. necessary to change the order in which those segments are linked together relative to the order in which corresponding segments are normally present in the parent polypeptide. In this regard, such overlapping segments when linked together in the synthetic polypeptide can adopt a different structure relative to the structure of the parent polypeptide, wherein the different structure does not provide for one or more functions associated with the parent polypeptide. For example, in the case of four segments A-B-C-D each spanning 30 contiguous amino acids of the parent polypeptide and having a 10-amino acid overlapping sequence with one or more adjacent segments, the synthetic polypeptide will have duplicated 10-amino acid sequences bridging segments A-B, B-C and C-D. The presence of these duplicated sequences may be sufficient to render a different structure and to abrogate or alter function relative to the parent polypeptide.

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In a preferred embodiment, segment size is about 30 amino acids and sequence overlap at one or both ends of a respective segment is about 15 amino acids. However, it will be understood that other suitable segment sizes and sequence overlap sizes are contemplated by the present invention, which can be readily ascertained by persons of skill in the art.

It is preferable but not necessary to utilise all the segments of the parent polypeptide in the construction of the synthetic polypeptide. Suitably, at least 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80% and still even more preferably at least 90% of the parent polypeptide sequence is used in the construction of the synthetic polypeptide. However, it will be understood that the more sequence information from a parent polypeptide that is utilised to construct the synthetic polypeptide, the greater the population coverage will be of the synthetic polypeptide as an immunogen. Preferably, no sequence information from the parent polypeptide is excluded (e.g., because of an apparent lack of immunological epitopes).

Persons of skill in the art will appreciate that when preparing a synthetic polypeptide against a pathogenic organism (e.g., a virus) or a cancer, it may be preferable to use sequence information from a plurality of different polypeptides expressed by the organism or the cancer. Accordingly, in a preferred embodiment, segments from a plurality of different polypeptides are linked together to form a synthetic polypeptide according to the invention. It is preferable in this respect to utilise as many parent polypeptides as possible from, or in relation to, a particular source in the construction of the synthetic polypeptide. The source of parent polypeptides includes, but is not limited to, a pathogenic organism and a cancer. Suitably, at least about 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80% and still even more preferably at least 90% of the parent polypeptides expressed by the source is used in the construction of the synthetic polypeptide. Preferably, parent polypeptides from a virus include, but are not restricted to, latent polypeptides, regulatory polypeptides or polypeptides expressed early during their replication cycle. Suitably, parent polypeptides from a parasite or bacterium include, but are not restricted to, secretory polypeptides and polypeptides expressed on the surface of

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the parasite or bacteria. It is preferred that parent polypeptides from a cancer or tumour are cancer specific polypeptides.

Suitably, hypervariable sequences within the parent polypeptide are excluded from the construction of the synthetic polypeptide.

The synthetic polypeptides of the inventions may be prepared by any suitable procedure known to those of skill in the art. For example, the polypeptide may be synthesised using solution synthesis or solid phase synthesis as described, for example, in Chapter 9 of Atherton and Shephard (1989, Solid Phase Peptide Synthesis: A Practical Approach. IRL Press, Oxford) and in Roberge et al (1995, Science 269: 202). Syntheses may employ, for example, either t-butyloxycarbonyl (t-Boc) or 9-fluorenylmethyloxycarbonyl (Fmoc) chemistries (see Chapter 9.1, of Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE, John Wiley & Sons, Inc. 1995-1997; Stewart and Young, 1984, Solid Phase Peptide Synthesis, 2nd ed. Pierce Chemical Co., Rockford, Ill; and Atherton and Shephard, supra).

Alternatively, the polypeptides may be prepared by a procedure including the steps of:

- (a) preparing a synthetic construct including a synthetic polynucleotide encoding a synthetic polypeptide wherein said synthetic polynucleotide is operably linked to a regulatory polynucleotide, wherein said synthetic polypeptide comprises a plurality of different segments of a parent polypeptide, wherein said segments are linked together in a different relationship relative to their linkage in the parent polypeptide;
 - (b) introducing the synthetic construct into a suitable host cell;
- (c) culturing the host cell to express the synthetic polypeptide from said synthetic construct; and
 - (d) isolating the synthetic polypeptide.

The synthetic construct is preferably in the form of an expression vector. For example, the expression vector can be a self-replicating extra-chromosomal vector such as a plasmid, or a vector that integrates into a host genome. Typically, the regulatory polynucleotide may include, but is not limited to, promoter sequences, leader or signal

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sequences, ribosomal binding sites, transcriptional start and stop sequences, translational start and termination sequences, and enhancer or activator sequences. Constitutive or inducible promoters as known in the art are contemplated by the invention. The promoters may be either naturally occurring promoters, or hybrid promoters that combine elements of more than one promoter. The regulatory polynucleotide will generally be appropriate for the host cell used for expression. Numerous types of appropriate expression vectors and suitable regulatory polynucleotides are known in the art for a variety of host cells.

In a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

The expression vector may also include a fusion partner (typically provided by the expression vector) so that the synthetic polypeptide of the invention is expressed as a fusion polypeptide with said fusion partner. The main advantage of fusion partners is that they assist identification and/or purification of said fusion polypeptide. In order to express said fusion polypeptide, it is necessary to ligate a polynucleotide according to the invention into the expression vector so that the translational reading frames of the fusion partner and the polynucleotide coincide.

Well known examples of fusion partners include, but are not limited to, glutathione-S-transferase (GST), Fc portion of human IgG, maltose binding protein (MBP) and hexahistidine (HIS₆), which are particularly useful for isolation of the fusion polypeptide by affinity chromatography. For the purposes of fusion polypeptide purification by affinity chromatography, relevant matrices for affinity chromatography are glutathione-, amylose-, and nickel- or cobalt-conjugated resins respectively. Many such matrices are available in "kit" form, such as the QIAexpressTM system (Qiagen) useful with (HIS₆) fusion partners and the Pharmacia GST purification system. In a preferred embodiment, the recombinant polynucleotide is expressed in the commercial vector pFLAGTM.

Another fusion partner well known in the art is green fluorescent protein (GFP). This fusion partner serves as a fluorescent "tag" which allows the fusion polypeptide of the invention to be identified by fluorescence microscopy or by flow cytometry. The GFP tag is useful when assessing subcellular localisation of a fusion polypeptide of the invention,

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or for isolating cells which express a fusion polypeptide of the invention. Flow cytometric methods such as fluorescence activated cell sorting (FACS) are particularly useful in this latter application. Preferably, the fusion partners also have protease cleavage sites, such as for Factor Xa, Thrombin and inteins (protein introns), which allow the relevant protease to partially digest the fusion polypeptide of the invention and thereby liberate the recombinant polypeptide of the invention therefrom. The liberated polypeptide can then be isolated from the fusion partner by subsequent chromatographic separation. Fusion partners according to the invention also include within their scope "epitope tags", which are usually short peptide sequences for which a specific antibody is available. Well known examples of epitope tags for which specific monoclonal antibodies are readily available include c-Myc, influenza virus, haemagglutinin and FLAG tags. Alternatively, a fusion partner may be provided to promote other forms of immunity. For example, the fusion partner may be an antigen-binding molecule that is immuno-interactive with a conformational epitope on a target antigen or to a post-translational modification of a target antigen (e.g., an antigen-binding molecule that is immuno-interactive with a glycosylated target antigen).

The step of introducing the synthetic construct into the host cell may be effected by any suitable method including transfection, and transformation, the choice of which will be dependent on the host cell employed. Such methods are well known to those of skill in the art.

Synthetic polypeptides of the invention may be produced by culturing a host cell transformed with the synthetic construct. The conditions appropriate for protein expression will vary with the choice of expression vector and the host cell. This is easily ascertained by one skilled in the art through routine experimentation.

Suitable host cells for expression may be prokaryotic or eukaryotic. One preferred host cell for expression of a polypeptide according to the invention is a bacterium. The bacterium used may be *Escherichia coli*. Alternatively, the host cell may be an insect cell such as, for example, *SF9* cells that may be utilised with a baculovirus expression system.

The synthetic polypeptide may be conveniently prepared by a person skilled in the art using standard protocols as for example described in Sambrook, et al., MOLECULAR CLONING. A LABORATORY MANUAL (Cold Spring Harbor Press, 1989), in particular

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Sections 16 and 17; Ausubel et al., CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (John Wiley & Sons, Inc. 1994-1998), in particular Chapters 10 and 16; and Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE (John Wiley & Sons, Inc. 1995-1997), in particular Chapters 1, 5 and 6.

The amino acids of the synthetic polypeptide can be any non-naturally occurring or any naturally occurring amino acid. Examples of unnatural amino acids and derivatives during peptide synthesis include but are not limited to, use of 4-amino butyric acid, 6-aminohexanoic acid, 4-amino-3-hydroxy-5-phenylpentanoic acid, 4-amino-3-hydroxy-6-methylheptanoic acid, t-butylglycine, norleucine, norvaline, phenylglycine, ornithine, sarcosine, 2-thienyl alanine and/or D-isomers of amino acids. A list of unnatural amino acids contemplated by the present invention is shown in TABLE C.

TABLE C

Non-conventional amino acid	Non-conventional amino acid
α-aminobutyric acid	L-N-methylalanine
α-amino-α-methylbutyrate	L-N-methylarginine
aminocyclopropane-carboxylate	L-N-methylasparagine
aminoisobutyric acid	L-N-methylaspartic acid
aminonorbornyl-carboxylate	L-N-methylcysteine
cyclohexylalanine	L-N-methylglutamine
cyclopentylalanine	L-N-methylglutamic acid
L-N-methylisoleucine	L-N-methylhistidine
D-alanine	L-N-methylleucine
D-arginine	L-N-methyllysine
D-aspartic acid	L-N-methylmethionine
D-cysteine	L-N-methylnorleucine
D-glutamate	L-N-methylnorvaline
D-glutamic acid	L-N-methylomithine

Non-conventional amino acid	Non-conventional amino acid
D-histidine	L-N-methylphenylalanine
D-isoleucine	L-N-methylproline
D-leucine	L-N-medlylserine
D-lysine	L-N-methylthreonine
D-methionine	L-N-methyltryptophan
D-omithine	L-N-methyltyrosine
D-phenylalanine	L-N-methylvaline
D-proline	L-N-methylethylglycine
D-serine	L-N-methyl-t-butylglycine
D-threonine	L-norleucine
D-tryptophan	L-norvaline
D-tyrosine	α-methyl-aminoisobutyrate
D-valine	α-methyl-γ-aminobutyrate
D-α-methylalanine	α-methylcyclohexylalanine
D-α-methylarginine	α-methylcylcopentylalanine
D-α-methylasparagine	α-methyl-α-napthylalanine
D-α-methylaspartate	α-methylpenicillamine
D-α-methylcysteine	N-(4-aminobutyl)glycine
D-α-methylglutamine	N-(2-aminoethyl)glycine
D-α-methylhistidine	N-(3-aminopropyl)glycine
D-α-methylisoleucine	N-amino-α-methylbutyrate
D-α-methylleucine	α-napthylalanine
D-α-methyllysine	N-benzylglycine
D-α-methylmethionine	N-(2-carbamylediyl)glycine
D-α-methylomithiine	N-(carbamylmethyl)glycine

Non-conventional amino acid	Non-conventional amino acid
D-α-methylphenylalanine	N-(2-carboxyethyl)glycine
D-α-methylproline	N-(carboxymethyl)glycine
D-α-methylserine	N-cyclobutylglycine
D-α-methylthreonine	N-cycloheptylglycine
D-α-methyltryptophan	N-cyclohexylglycine
D-α-methyltyrosine	N-cyclodecylglycine
L-α-methylleucine	L-α-methyllysine
L-\alpha-methylmethionine	L-α-methylnorleucine
L-o-methylnorvatine	L-α-methylornithine
L-α-methylphenylalanine	L-α-methylproline
L-α-methylserine	L-α-methylthreonine
L-α-methyltryptophan	L-α-methyltyrosine
L-α-methylvaline	L-N-methylhomophenylalanine
N-(N-(2,2-diphenylethyl carbamylmethyl)glycine	N-(N-(3,3-diphenylpropyl carbamylmethyl)glycine
1-carboxy-1-(2,2-diphenyl-ethyl amino)cyclopropane	

The invention also contemplates modifying the synthetic polypeptides of the invention using ordinary molecular biological techniques so as to alter their resistance to proteolytic degradation or to optimise solubility properties or to render them more suitable as an immunogenic agent.

3. Preparation of synthetic polynucleotides of the invention

The invention contemplates synthetic polynucleotides encoding the synthetic polypeptides as for example described in Section 2 supra. Polynucleotides encoding segments of a parent polypeptide can be produced by any suitable technique. For example, such polynucleotides can be synthesised de novo using readily available machinery.

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Sequential synthesis of DNA is described, for example, in U.S. Patent No 4,293,652. Instead of *de novo* synthesis, recombinant techniques may be employed including use of restriction endonucleases to cleave a polynucleotide encoding at least a segment of the parent polypeptide and use of ligases to ligate together in frame a plurality of cleaved polynucleotides encoding different segments of the parent polypeptide. Suitable recombinant techniques are described for example in the relevant sections of Ausubel, *et al.* (*supra*) and of Sambrook, *et al.*, (*supra*) which are incorporated herein by reference. Preferably, the synthetic polynucleotide is constructed using splicing by overlapping extension (SOEing) as for example described by Horton *et al.* (1990, *Biotechniques* 8(5): 528-535; 1995, *Mol Biotechnol.* 3(2): 93-99; and 1997, *Methods Mol Biol.* 67: 141-149). However, it should be noted that the present invention is not dependent on, and not directed to, any one particular technique for constructing the synthetic construct.

Various modifications to the synthetic polynucleotides may be introduced as a means of increasing intracellular stability and half-life. Possible modifications include but are not limited to the addition of flanking sequences of ribo- or deoxy- nucleotides to the 5' and/or 3' ends of the molecule or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the oligodeoxyribonucleotide backbone.

The invention therefore contemplates a method of producing a synthetic polynucleotide as broadly described above, comprising linking together in the same reading frame at least two nucleic acid sequences encoding different segments of a parent polypeptide to form a synthetic polynucleotide, which encodes a synthetic polypeptide according to the invention. Suitably, nucleic acid sequences encoding at least 10 segments, preferably at least 20 segments, more preferably at least 40 segments and more preferably at least 100 segments of a parent polypeptide are employed to produce the synthetic polynucleotide.

Preferably, the method further comprises selecting segments of the parent polypeptide, reverse translating the selected segments and preparing nucleic acid sequences encoding the selected segments. It is preferred that the method further comprises randomly linking the nucleic acid sequences together to form the synthetic polynucleotide. The nucleic acid sequences may be oligonucleotides or polynucleotides.

Suitably, segments are selected on the basis of size. Additionally, or in the alternative, segments are selected such that they have partial sequence identity or homology (i.e., sequence overlap) with one or more other segments. A number of factors can influence segment size and sequence overlap as mentioned above. In the case of sequence overlap, large amounts of duplicated nucleic acid sequences can sometimes result in sections of nucleic acid being lost during nucleic acid amplification (e.g., polymerase chain reaction, PCR) of such sequences, recombinant plasmid propagation in a bacterial host or during amplification of recombinant viruses containing such sequences. Accordingly, in a preferred embodiment, nucleic acid sequences encoding segments having sequence identity or homology with one or more other encoded segments are not linked together in an arrangement in which the identical or homologous sequences are contiguous. Also, it is preferable that different codons are used to encode a specific amino acid in a duplicated region. In this context, an amino acid of a parent polypeptide sequence is preferably reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence (e.g., a duplicated sequence or a palindromic sequence) that is refractory to the execution of a task (e.g., cloning or sequencing). Alternatively, segments may be selected such that they contain a carboxyl terminal leucine residue or such that reverse translated sequences encoding the segments contain restriction enzyme sites for convenient splicing of the reverse translated sequences.

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The method optionally further comprises linking a spacer oligonucleotide encoding at least one spacer residue between segment-encoding nucleic acids. Such spacer residue(s) may be advantageous in ensuring that epitopes within the segments are processed and presented efficiently. Preferably, the spacer oligonucleotide encodes 2 to 3 spacer residues. The spacer residue is suitably a neutral amino acid, which is preferably alanine.

Optionally, the method further comprises linking in the same reading frame as other segment-containing nucleic acid sequences at least one variant nucleic acid sequence which encodes a variant segment having a homologous but not identical amino acid sequence relative to other encoded segments. Suitably, the variant segment comprises conserved and/or non-conserved amino acid differences relative to one or more other encoded segments. Such differences may correspond to polymorphisms as discussed

above. In a preferred embodiment, degenerate bases are designed or built in to the at least one variant nucleic acid sequence to give rise to all desired homologous sequences.

When a large number of polymorphisms is intended to be covered, it is preferred that multiple synthetic polynucleotides are constructed rather than a single synthetic polynucleotide, which encodes all variant segments. For example, if there is less than 85% homology between polymorphic polypeptides, then it is preferred that more than one synthetic polynucleotide is constructed.

Preferably, the method further comprises optimising the codon composition of the synthetic polynucleotide such that it is translated efficiently by a host cell. In this regard, it is well known that the translational efficiency of different codons varies between organisms and that such differences in codon usage can be utilised to enhance the level of protein expression in a particular organism. In this regard, reference may be made to Seed et al. (International Application Publication No WO 96/09378) who disclose the replacement of existing codons in a parent polynucleotide with synonymous codons to enhance expression of viral polypeptides in mammalian host cells. Preferably, the first or second most frequently used codons are employed for codon optimisation.

Preferably, gene splicing by overlap extension or "gene SOEing" (supra) is employed for the construction of the synthetic polynucleotide which is a PCR-based method of recombining DNA sequences without reliance on restriction sites and of directly generating mutated DNA fragments in vitro. By modifying the sequences incorporated into the 5'-ends of the primers, any pair of PCR products can be made to share a common sequence at one end. Under PCR conditions, the common sequence allows strands from two different fragments to hybridise to one another, forming an overlap. Extension of this overlap by DNA polymerase yields a recombinant molecule. However, a problem with long synthetic constructs is that mutations generally incorporate into amplified products during synthesis. In this instance, it is preferred that resolvase treatment is employed at various steps of the synthesis. Resolvases are bacteriophage-encoded endonucleases which recognise disruptions or mispairing of double stranded DNA and are primarily used by bacteriophages to resolve Holliday junctions (Mizuuchi, 1982; Youil et al., 1995). For example, T7 endonuclease I can be employed in synthetic DNA constructions to recognise mutations and cleave corrupted dsDNA. The mutated DNA strands are then hybridised to

non-mutant or correct DNA sequences, which results in a mispairing of DNA bases. The mispaired bases are recognised by the resolvase, which then cleaves the DNA nearby leaving only correctly hybridised sequences intact. Preferably a thermostable resolvase enzyme is employed during splicing or amplification so that errors are not incorporated in downstream synthesis products.

Synthetic polynucleotides according to the invention can be operably linked to a regulatory polynucleotide in the form a synthetic construct as for example described in Section 2 supra. Synthetic constructs of the invention have utility inter alia as nucleic acid vaccines. The choice of regulatory polynucleotide and synthetic construct will depend on the intended host.

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Exemplary expression vectors for expression of a synthetic polypeptide according to the invention include, but are not restricted to, modified Ankara Vaccinia virus as for example described by Allen et al. (2000, J. Immunol. 164(9): 4968-4978), fowlpox virus as for example described by Boyle and Coupar (1988, Virus Res. 10: 343-356) and the herpes simplex amplicons described for example by Fong et al. in U.S. Patent No. 6,051,428. Alternatively, Adenovirus and Epstein-Barr virus vectors, which are preferably capable of accepting large amounts of DNA or RNA sequence information, can be used.

Preferred promoter sequences that can be utilised for expression of synthetic polypeptides include the P7.5 or PE/L promoters as for example disclosed by Kumar and Boyle. (1990, *Virology* 179: 151-158), CMV and RSV promoters.

The synthetic construct optionally further includes a nucleic acid sequence encoding an immunostimulatory molecule. The immunostimulatory molecule may be fusion partner of the synthetic polypeptide. Alternatively, the immunostimulatory molecule may be translated separately from the synthetic polypeptide. Preferably, the immunostimulatory molecule comprises a general immunostimulatory peptide sequence. For example, the immunostimulatory peptide sequence may comprise a domain of an invasin protein (Inv) from the bacteria *Yersinia* spp as for example disclosed by Brett *et al.* (1993, *Eur. J. Immunol.* 23: 1608-1614). This immune stimulatory property results from the capability of this invasin domain to interact with the β 1 integrin molecules present on T cells, particularly activated immune or memory T cells. A preferred embodiment of the invasin domain (Inv) for linkage to a synthetic polypeptide has been previously described

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in U.S. Pat. No. 5,759,551. The said Inv domain has the sequence: Thr-Ala-Lys-Ser-Lys-Lys-Phe-Pro-Ser-Tyr-Thr-Ala-Thr-Tyr-Gln-Phe [SEQ ID NO; 1467] or is an immune stimulatory homologue thereof from the corresponding region in another Yersinia species invasin protein. Such homologues thus may contain substitutions, deletions or insertions of amino acid residues to accommodate strain to strain variation, provided that the homologues retain immune stimulatory properties. The general immunostimulatory sequence may optionally be linked to the synthetic polypeptide by a spacer sequence.

In an alternate embodiment, the immunostimulatory molecule may comprise an immunostimulatory membrane or soluble molecule, which is suitably a T cell costimulatory molecule. Preferably, the T cell co-stimulatory molecule is a B7 molecule or a biologically active fragment thereof, or a variant or derivative of these. The B7 molecule includes, but is not restricted to, B7-1 and B7-2. Preferably, the B7 molecule is B7-1. Alternatively, the T cell co-stimulatory molecule may be an ICAM molecule such as ICAM-1 and ICAM-2.

In another embodiment, the immunostimulatory molecule can be a cytokine, which includes, but is not restricted to, an interleukin, a lymphokine, tumour necrosis factor and an interferon. Alternatively, the immunostimulatory molecule may comprise an immunomodulatory oligonucleotide as for example disclosed by Krieg in U.S. Patent No. 6,008,200.

Suitably, the size of the synthetic polynucleotide does not exceed the ability of host cells to transcribe, translate or proteolytically process and present epitopes to the immune system. Practitioners in the art will also recognise that the size of the synthetic polynucleotide can impact on the capacity of an expression vector to express the synthetic polynucleotide in a host cell. In this connection, it is known that the efficacy of DNA vaccination reduces with expression vectors greater that 20-kb. In such situations it is preferred that a larger number of smaller synthetic constructs is utilised rather than a single large synthetic construct.

4. Immunopotentiating compositions

The invention also contemplates a composition, comprising an 30 immunopotentiating agent selected from the group consisting of a synthetic polypeptide as

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described in Section 2, and a synthetic polynucleotide or a synthetic construct as described in Section 3, together with a pharmaceutically acceptable carrier. One or more immunopotentiating agents can be used as actives in the preparation of immunopotentiating compositions. Such preparation uses routine methods known to persons skilled in the art. Typically, such compositions are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid prior to injection may also be prepared. The preparation may also be emulsified. The active immunogenic ingredients are often mixed with excipients that are pharmaceutically acceptable and compatible with the active ingredient. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol, or the like and combinations thereof. In addition, if desired, the vaccine may contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, and/or adjuvants that enhance the effectiveness of the vaccine. Examples of adjuvants which may be effective include but are not limited to: aluminium hydroxide, N-acetyl-muramyl-L-threonyl-D-isoglutamine (thur-MDP), Nacetyl-nor-muramyl-L-alanyl-D-isoglutamine (CGP 11637, referred to as nor-MDP), Nacetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3hydroxyphosphoryloxy)-ethylamine (CGP 1983A, referred to as MTP-PE), and RIBI, which contains three components extracted from bacteria, monophosphoryl lipid A, trehalose dimycolate and cell wall skeleton (MPL+TDM+CWS) in a 2% squalene/Tween 80 emulsion. For example, the effectiveness of an adjuvant may be determined by measuring the amount of antibodies resulting from the administration of the composition, wherein those antibodies are directed against one or more antigens presented by the treated cells of the composition.

The immunopotentiating agents may be formulated into a composition as neutral or salt forms. Pharmaceutically acceptable salts include the acid addition salts (formed with free amino groups of the peptide) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids such as acetic, oxalic, tartaric, maleic, and the like. Salts formed with the free carboxyl groups may also be derived from inorganic basis such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic basis as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

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If desired, devices or compositions containing the immunopotentiating agents suitable for sustained or intermittent release could be, in effect, implanted in the body or topically applied thereto for the relatively slow release of such materials into the body.

The compositions are conventionally administered parenterally, by injection, for example, either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories and, in some cases, oral formulations. For suppositories, traditional binders and carriers may include, for example, polyalkylene glycols or triglycerides; such suppositories may be formed from mixtures containing the active ingredient in the range of 0.5% to 10%, preferably 1%-2%. Oral formulations include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium carbonate, and the like. These compositions take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain 10%-95% of active ingredient, preferably 25%-70%.

Administration of the gene therapy construct to said mammal, preferably a human, may include delivery via direct oral intake, systemic injection, or delivery to selected tissue(s) or cells, or indirectly via delivery to cells isolated from the mammal or a compatible donor. An example of the latter approach would be stem cell therapy, wherein isolated stem cells having potential for growth and differentiation are transfected with the vector comprising the *Sox18* nucleic acid. The stem cells are cultured for a period and then transferred to the mammal being treated.

With regard to nucleic acid based compositions, all modes of delivery of such compositions are contemplated by the present invention. Delivery of these compositions to cells or tissues of an animal may be facilitated by microprojectile bombardment, liposome mediated transfection (e.g., lipofectin or lipofectamine), electroporation, calcium phosphate or DEAE-dextran-mediated transfection, for example. In an alternate embodiment, a synthetic construct may be used as a therapeutic or prophylactic composition in the form of a "naked DNA" composition as is known in the art. A discussion of suitable delivery methods may be found in Chapter 9 of CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (Eds. Ausubel et al.; John Wiley & Sons Inc., 1997 Edition) or on the Internet site DNAvaccine.com. The compositions may be administered by intradermal (e.g., using panjetTM delivery) or intramuscular routes.

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The step of introducing the synthetic polynucleotide into a target cell will differ depending on the intended use and species, and can involve one or more of non-viral and viral vectors, cationic liposomes, retroviruses, and adenoviruses such as, for example, described in Mulligan, R.C., (1993 *Science* 260 926-932) which is hereby incorporated by reference. Such methods can include, for example:

- A. Local application of the synthetic polynucleotide by injection (Wolff et al., 1990, Science 247 1465-1468, which is hereby incorporated by reference), surgical implantation, instillation or any other means. This method can also be used in combination with local application by injection, surgical implantation, instillation or any other means, of cells responsive to the protein encoded by the synthetic polynucleotide so as to increase the effectiveness of that treatment. This method can also be used in combination with local application by injection, surgical implantation, instillation or any other means, of another factor or factors required for the activity of said protein.
- B. General systemic delivery by injection of DNA, (Calabretta et al., 1993, Cancer Treat. Rev. 19 169-179, which is incorporated herein by reference), or RNA, alone or in combination with liposomes (Zhu et al., 1993, Science 261 209-212, which is incorporated herein by reference), viral capsids or nanoparticles (Bertling et al., 1991, Biotech. Appl. Biochem. 13 390-405, which is incorporated herein by reference) or any other mediator of delivery. Improved targeting might be achieved by linking the synthetic polynucleotide to a targeting molecule (the so-called "magic bullet" approach employing, for example, an antibody), or by local application by injection, surgical implantation or any other means, of another factor or factors required for the activity of the protein encoding said synthetic polynucleotide, or of cells responsive to said protein.
 - C. Injection or implantation or delivery by any means, of cells that have been modified ex vivo by transfection (for example, in the presence of calcium phosphate: Chen et al., 1987, Mole. Cell Biochem. 7 2745-2752, or of cationic lipids and polyamines: Rose et al., 1991, BioTech. 10 520-525, which articles are incorporated herein by reference), infection, injection, electroporation (Shigekawa et al., 1988, BioTech. 6 742-751, which is incorporated herein by reference) or any other way so as to increase the

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expression of said synthetic polynucleotide in those cells. The modification can be mediated by plasmid, bacteriophage, cosmid, viral (such as adenoviral or retroviral; Mulligan, 1993, Science 260 926-932; Miller, 1992, Nature 357 455-460; Salmons et al., 1993, Hum. Gen. Ther. 4 129-141, which articles are incorporated herein by reference) or other vectors, or other agents of modification such as liposomes (Zhu et al., 1993, Science 261 209-212, which is incorporated herein by reference), viral capsids or nanoparticles (Bertling et al., 1991, Biotech. Appl. Biochem. 13 390-405, which is incorporated herein by reference), or any other mediator of modification. The use of cells as a delivery vehicle for genes or gene products has been described by Barr et al., 1991, Science 254 1507-1512 and by Dhawan et al., 1991, Science 254 1509-1512, which articles are incorporated herein by reference. Treated cells can be delivered in combination with any nutrient, growth factor, matrix or other agent that will promote their survival in the treated subject.

Also encapsulated by the present invention is a method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment a therapeutically effective amount of a composition as broadly described above. The disease or condition may be caused by a pathogenic organism or a cancer as for example described above.

In a preferred embodiment, the immunopotentiating composition of the invention is suitable for treatment of, or prophylaxis against, a cancer. Cancers which could be suitably treated in accordance with the practices of this invention include cancers of the lung, breast, ovary, cervix, colon, head and neck, pancreas, prostate, stomach, bladder, kidney, bone liver, oesophagus, brain, testicle, uterus, melanoma and the various leukemias and lymphomas.

In an alternate embodiment, the immunopotentiating composition is suitable for treatment of, or prophylaxis against, a viral, bacterial or parasitic infection. Viral infections contemplated by the present invention include, but are not restricted to, infections caused by HIV, Hepatitis, Influenza, Japanese encephalitis virus, Epstein-Barr virus and respiratory syncytial virus. Bacterial infections include, but are not restricted to, those caused by Neisseria species, Meningococcal species, Haemophilus species Salmonella species, Streptococcal species, Legionella species and Mycobacterium species. Parasitic

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infections encompassed by the invention include, but are not restricted to, those caused by *Plasmodium* species, *Schistosoma* species, *Leishmania* species, *Trypanosoma* species, *Toxoplasma* species and *Giardia* species.

The above compositions or vaccines may be administered in a manner compatible with the dosage formulation, and in such amount as is therapeutically effective to alleviate patients from the disease or condition or as is prophylactically effective to prevent incidence of the disease or condition in the patient. The dose administered to a patient, in the context of the present invention, should be sufficient to effect a beneficial response in a patient over time such as a reduction or cessation of blood loss. The quantity of the composition or vaccine to be administered may depend on the subject to be treated inclusive of the age, sex, weight and general health condition thereof. In this regard, precise amounts of the composition or vaccine for administration will depend on the judgement of the practitioner. In determining the effective amount of the composition or vaccine to be administered in the treatment of a disease or condition, the physician may evaluate the progression of the disease or condition over time. In any event, those of skill in the art may readily determine suitable dosages of the composition or vaccine of the invention.

In a preferred embodiment, DNA-based immunopotentiating agent (e.g., 100 μ g) is delivered intradermally into a patient at day 1 and at week 8 to prime the patient. A recombinant poxvirus (e.g., at 10^7 pfu/mL) from which substantially the same immunopotentiating agent can be expressed is then delivered intradermally as a booster at weeks 16 and 24, respectively.

The effectiveness of the immunisation may be assessed using any suitable technique. For example, CTL lysis assays may be employed using stimulated splenocytes or peripheral blood mononuclear cells (PBMC) on peptide coated or recombinant virus infected cells using ⁵¹Cr labelled target cells. Such assays can be performed using for example primate, mouse or human cells (Allen et al., 2000, J. Immunol. 164(9): 4968-4978 also Woodberry et al., infra). Alternatively, the efficacy of the immunisation may be monitored using one or more techniques including, but not limited to, HLA class I Tetramer staining - of both fresh and stimulated PBMCs (see for example Allen et al., supra), proliferation assays (Allen et al., supra), ElispotTM Assays and intracellular INF-

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gamma staining (Allen et al., supra), ELISA Assays - for linear B cell responses; and Western blots of cell sample expressing the synthetic polynucleotides.

5. Computer related embodiments

The design or construction of a synthetic polypeptide sequence or a synthetic polynucleotide sequence according to the invention is suitably facilitated with the assistance of a computer programmed with software, which inter alia fragments a parent sequence into fragments, and which links those fragments together in a different relationship relative to their linkage in the parent sequence. The ready use of a parent sequence for the construction of a desired synthetic molecule according to the invention requires that it be stored in a computer-readable format. Thus, in accordance with the present invention, sequence data relating to a parent molecule (e.g., a parent polypeptide) is stored in a machine-readable storage medium, which is capable of processing the data to fragment the sequence of the parent molecule into fragments and to link together the fragments in a different relationship relative to their linkage in the parent molecule.

Therefore, another embodiment of the present invention provides a machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when used by a machine programmed with instructions for using said data, fragments a parent sequence into fragments, and links those fragments together in a different relationship relative to their linkage in the parent sequence. In a preferred embodiment of this type, a machine-readable data storage medium is provided that is capable of reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding the fragment and to link together in the same reading frame each of the nucleic acid sequences to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in a parent polypeptide sequence.

In another embodiment, the invention encompasses a computer for designing the sequence of a synthetic polypeptide and/or a synthetic polynucleotide of the invention, wherein the computer comprises wherein said computer comprises: (a) a machine readable data storage medium comprising a data storage material encoded with machine readable data, wherein said machine readable data comprises the sequence of a parent polypeptide; (b) a working memory for storing instructions for processing said machine-readable data;

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(c) a central-processing unit coupled to said working memory and to said machine-readable data storage medium, for processing said machine-readable data into said synthetic polypeptide sequence and/or said synthetic polynucleotide; and (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence and/or said synthetic polynucleotide.

In yet another embodiment, the invention contemplates a computer program product for designing the sequence of a synthetic polynucleotide of the invention, comprising code that receives as input the sequence of a parent polypeptide, code that fragments the sequence of the parent polypeptide into fragments, code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding the fragment, code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the parent polypeptide sequence, and a computer readable medium that stores the codes.

A version of these embodiments is presented in Figure 23, which shows a system 10 including a computer 11 comprising a central processing unit ("CPU") 20, a working memory 22 which may be, e.g., RAM (random-access memory) or "core" memory, mass storage memory 24 (such as one or more disk drives or CD-ROM drives), one or more cathode-ray tube ("CRT") display terminals 26, one or more keyboards 28, one or more input lines 30, and one or more output lines 40, all of which are interconnected by a conventional bidirectional system bus 50.

Input hardware 36, coupled to computer 11 by input lines 30, may be implemented in a variety of ways. For example, machine-readable data of this invention may be inputted via the use of a modem or modems 32 connected by a telephone line or dedicated data line 34. Alternatively or additionally, the input hardware 36 may comprise CD. Alternatively, ROM drives or disk drives 24 in conjunction with display terminal 26, keyboard 28 may also be used as an input device.

Output hardware 46, coupled to computer 11 by output lines 40, may similarly be implemented by conventional devices. By way of example, output hardware 46 may include CRT display terminal 26 for displaying a synthetic polynucleotide sequence or a synthetic polypeptide sequence as described herein. Output hardware might also include a

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printer 42, so that hard copy output may be produced, or a disk drive 24, to store system output for later use.

In operation, CPU 20 coordinates the use of the various input and output devices 36,46 coordinates data accesses from mass storage 24 and accesses to and from working memory 22, and determines the sequence of data processing steps. A number of programs may be used to process the machine readable data of this invention. Exemplary programs may use for example the steps outlined in the flow diagram illustrated in Figure 24. Broadly, these steps include (1) inputting at least one parent polypeptide sequence; (2) optionally adding to alanine spacers at the ends of each polypeptide sequence; (3) fragmenting the polypeptide sequences into fragments (e.g., 30 amino acids long), which are preferably overlapping (e.g., by 15 amino acids); (4) reverse translating the fragment to provide a nucleic acid sequence for each fragment and preferably using for the reverse translation first and second most translationally efficient codons for a cell type, wherein the codons are preferably alternated out of frame with each other in the overlaps of consecutive fragments; (5) randomly rearranging the fragments; (6) checking whether rearranged fragments recreate at least a portion of a parent polypeptide sequence; (7) repeating randomly rearranging the fragments when rearranged fragments recreate said at least a portion; or otherwise (8) linking the rearranged fragments together to produce a synthetic polypeptide sequence and/or a synthetic polynucleotide sequence; and (9) outputting said synthetic polypeptide sequence and/or a synthetic polynucleotide sequence. An example of an algorithm which uses inter alia the aforementioned steps is shown in Figure 25. By way of example, this algorithm has been used for the design of synthetic polynucleotides and synthetic polypeptides according to the present invention for Hepatitis C 1a and for melanoma, as illustrated in Figures 26 and 27.

Figure 28 shows a cross section of a magnetic data storage medium 100 which can be encoded with machine readable data, or set of instructions, for designing a synthetic molecule of the invention, which can be carried out by a system such as system 10 of Figure 23. Medium 100 can be a conventional floppy diskette or hard disk, having a suitable substrate 101, which may be conventional, and a suitable coating 102, which may be conventional, on one or both sides, containing magnetic domains (not visible) whose polarity or orientation can be altered magnetically. Medium 100 may also have an opening (not shown) for receiving the spindle of a disk drive or other data storage device 24. The

magnetic domains of coating 102 of medium 100 are polarised or oriented so as to encode in manner which may be conventional, machine readable data such as that described herein, for execution by a system such as system 10 of Figure 23.

Figure 29 shows a cross section of an optically readable data storage medium 110 which also can be encoded with such a machine-readable data, or set of instructions, for designing a synthetic molecule of the invention, which can be carried out by a system such as system 10 of Figure 23. Medium 110 can be a conventional compact disk read only memory (CD-ROM) or a rewritable medium such as a magneto-optical disk, which is optically readable and magneto-optically writable. Medium 100 preferably has a suitable substrate 111, which may be conventional, and a suitable coating 112, which may be conventional, usually of one side of substrate 111.

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In the case of CD-ROM, as is well known, coating 112 is reflective and is impressed with a plurality of pits 113 to encode the machine-readable data. The arrangement of pits is read by reflecting laser light off the surface of coating 112. A protective coating 114, which preferably is substantially transparent, is provided on top of coating 112.

In the case of a magneto-optical disk, as is well known, coating 112 has no pits 113, but has a plurality of magnetic domains whose polarity or orientation can be changed magnetically when heated above a certain temperature, as by a laser (not shown). The orientation of the domains can be read by measuring the polarisation of laser light reflected from coating 112. The arrangement of the domains encodes the data as described above.

In order that the invention may be readily understood and put into practical effect, particular preferred non-limiting embodiments will now be described as follows.

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EXAMPLES

EXAMPLE 1

Preparation of an HIV Savine

Experimental Protocol

5 Plasmids

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The plasmid pDNAVacc is ampicillin resistant and contains an expression cassette comprising a CMV promoter and enhancer, a synthetic intron, a multiple cloning site (MCS) and a SV40poly A signal sequence (Thomson *et al.*, 1998). The plasmid pTK7.5 and contains a selection cassette, a pox virus 7.5 early/late promoter and a MCS flanked on either side by Vaccinia virus TK gene sequences.

Recombinant Vaccinia Viruses

Recombinant Vaccinia viruses expressing the gag, env (IIB) and pol (LAI) genes of HIV-1 were used as previously described and denoted VV-GAG, VV-POL, VV-ENV (Woodberry et al., 1999; Kent et al., 1998).

15 Marker Rescue Recombination

Recombinant Vaccinia viruses containing Savine constructs were generated by marker rescue recombination, using protocols described previously (Boyle et al., 1985). Plaque purified viruses were tested for the TK phenotype and for the appropriate genome arrangement by Southern blot and PCR.

20 Oligonucleotides

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Oligonucleotides 50 nmol scale and desalted were purchased from Life Technologies. Short oligonucleotides were resuspended in 100 μ L of water, their concentration determined, then diluted to 20 μ M for use in PCR or sequencing reactions. Long oligonucleotides for splicing reactions were denatured for 5 minutes at 94°C in 20 μ L of formamide loading buffer then 0.5 μ L gel purified on a 6% polyacrylamide gel.

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Gel slices containing full-length oligonucleotides were visualised with ethidium bromide, excised, placed in EppendorfTM tubes, combined with 200 µL of water before being crushed using the plunger of a 1 mL syringe. Before being used in splicing reactions the crushed gel was resuspended in an appropriate volume of buffer and 1-2 µL of the resuspendate used directly in the splicing reactions.

Sequencing

Sequencing was performed using Dye terminator sequencing reactions and analyzed by the Biomedical Resource Facility at the John Curtin School of Medical Research using an ABI automated sequencer.

10 Restimulation of Lymphocytes from HIV Infected Patients

Two pools of recombinant Vaccinia viruses containing VV-AC1 + VV-BC1 (Pool 1) or VV-AC2 + VV-BC2 + VV-CC2 (Pool 2) were used to restimulate lymphocytes from the blood samples of HIV-infected patients. Briefly CTL lines were generated from HIVinfected donor PBMC. A fifth of the total PBMC were infected with either Pool 1 or Pool 2 Vaccinia viruses then added back to the original cell suspension. The infected cell suspension was then cultured with IL-7 for 1 week.

CTL Assays

Restimulated PBMCs were used as effectors in a standard ⁵¹Cr-release CTL assay. Targets were autologous EBV-transformed lymphoblastoid cell lines (LCLs) infected with the following viruses: Pool 1, Pool 2, VV-GAG, VV-POL or VV-ENV. Assay controls included uninfected targets, targets infected with VV-lacZ (virus control) and K562 cells.

Results 1 4 1

HIV Savine Design

A main goal of the Savine strategy is to include as much protein sequence information from a pathogen or cancer as possible in such a way that potential T cell epitopes remain intact and so that the vaccine or therapy is extremely safe. An HIV Savine is described herein not only to compare this strategy to other strategies but also, to produce

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an HIV vaccine that would provide the maximum possible population coverage as well as catering for the major HIV clades.

A number of design criteria was first determined to exploit the many advantages of using a synthetic approach. One advantage is that it is possible to use consensus protein sequences to design these vaccines. Using consensus sequences for a highly variable virus like HIV should provide better vaccine coverage because individual viral isolate sequences may have lost epitopes which induce CTL against the majority of other viral isolates. Thus, using the consensus sequences of each HIV clade rather than individual isolate sequences should provide better vaccine coverage. Taking this one step further, a consensus sequence that covers all HIV clades should theoretically provide better coverage than using just the consensus sequences for individual clades. Before designing such a sequence however, it was decided that a more appropriate and focussed HIV vaccine might be constructed if the various clades were first ranked according to their relative importance. To establish such a ranking the following issues were considered, current prevalence of each clade, the rate at which each clade is increasing and the capacity of various regions of the world to cope with the HIV pandemic (Figures 1 and 2). These criteria produced the following ranking, Clade $E \ge \text{clade } A > \text{clade } C > \text{clade } B > \text{clade } D > \text{other clades. Clades } E \text{ and } A \text{ were}$ considered to almost equal since they are very similar except in their envelope protein sequences, which differ considerably.

Another advantage of synthesising a designed sequence is that it is possible to incorporate degenerate sequences into their design. In the case of HIV, this means that more than one amino acid can be included at various positions to improve the ability of the vaccine to cater for the various HIV clades and isolates. Coverage is improved because mutations in different HIV clades and also in individual isolate sequences, while mostly destroying specific T cell epitopes, can result in the formation of new potentially useful epitopes nearby (Goulder et al., 1997). Incorporating degenerate amino acid sequences, however, also means that more than one construct must be made and mixed together. The number of constructs required depends on the frequency with which mutations are incorporated into the design. While this approach requires the construction of additional constructs, these constructs can be prepared from the same set of degenerate long oligonucleotides, significantly reducing the cost of providing such considerable interclade coverage.

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A set of degeneracy rules was developed for the incorporation of amino acid mutations into the design which meant that a maximum of eight constructs would be required so that theoretically all combinations were present, as follows: 1) Two amino acids at three positions (or less) within any group of nine amino acids (*i.e.*, present in a CTL epitope); 2) Three amino acids at one position and two at another (or not) within any group of nine amino acids; 3) Four amino acids at one position and two at another (or not) within any group of nine amino acids. The reason why these rules were applied to nine amino acids (the average CTL epitope size) and not to larger stretches of amino acid sequence to cater for class II restricted epitopes, is because class II-restricted epitopes generally have a core sequence of nine amino acids in the middle which bind specifically to class II MHC molecules with the extra flanking sequences stabilising binding, by associating with either side of class II MHC antigens in a largely sequence independent manner (Brown et al., 1993).

Using the HIV clade ranking described above, the amino acid degeneracy rules and in some situations the similarity between amino acids, a degenerate consensus protein sequence was designed for each HIV protein using the consensus protein sequences for each HIV clade compiled by the Los Alamos HIV sequence database (Figures 3-11) (HIV Molecular Immunology Database, 1997). It is important to note that in some situations the order with which each of the above design criteria was applied was altered. Each time this was done the primary goal however was to increase the ability of the Savine to cater for interclade differences. Two isolate sequences, GenBank accession U51189 and U46016, for clade E and clade C, respectively, were used when a consensus sequence for some HIV proteins from these two clades was unavailable (Gao et al., 1996; Salminen et al., 1996). The design of a consensus sequence for the hypervariable regions of the HIV envelope protein and in some cases between these regions (hypervariable regions 1-2 and 3-5) was difficult and so these regions were excluded from the vaccine design.

Once a degenerate consensus sequence was designed for each HIV protein, an approach was then determined for incorporating all the protein sequences safely into the vaccine. One convenient approach to ensure that a vaccine will be safe is to systematically fragment and randomly rearrange the protein sequences together thus abrogating or otherwise altering their structure and function. The protein sequences still have to be immunologically functional however, meaning that the process used to fragment the

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sequences should not destroy potential epitopes. To decide on the best approach for systematically fragmenting protein sequences, the main criteria used was the size of T epitopes and their processing requirements. Class I-restricted T cell epitopes are 8-10 amino acids long and generally require 2-3 natural flanking amino acids to ensure their efficient processing and presentation if placed next to unnatural flanking residues (Del Val et al., 1991; Thomson et al., 1995). Class II-restricted T cell epitopes range between 12-25 amino acids long and do appear to require natural flanking residues for processing however, it is difficult to rule out a role for natural flanking residues in all cases due to the complexity of their processing pathways (Thomson et al., 1998). Also class II-restricted epitopes despite being larger than CTL epitopes generally have a core sequence of 9-10 amino acids, which binds to MHC molecules in a sequence specific fashion. Thus, based on current knowledge, it was decided that an advantageous approach was to overlap the fragments by at least 15 amino acids to ensure that potential epitopes which might lie across fragment boundaries are not lost and to ensure that CTL epitopes near fragment boundaries, that are placed beside or near inhibitory amino acids in adjacent fragments, are processed efficiently. In deciding the optimal fragment size, the main criteria used were that size had to be small enough to cause the maximum disruption to the structure and function of proteins but large enough to cover the sequence information as efficiently as possible without any further unnecessary duplication. Based on these criteria the fragments would be twice the overlap size, in this case 30 amino acids long.

The designed degenerate protein sequences were then separated into fragments 30 amino acid long and overlapping by fifteen amino acids. Two alanine amino acids were also added to the start and end of the first and last fragment for each protein or envelop protein segment to ensure these fragments were not placed directly adjacent to amino acids capable of blocking epitope processing (Del Val et al., 1991). The next step was to reverse translate each protein sequence back into DNA. Duplicating DNA sequences was avoided when constructing DNA sequences encoding a tandem repeat of identical or homologous amino acid sequences to maximise expression of the Savine. In this regard, the first and second most commonly used mammalian codons (shown in Figure 12) were assigned to amino acids in these repeat regions, wherein a first codon was used to encode an amino acid in one of the repeated sequences and wherein a second but synonymous codon was used for the other repeated sequence (e.g., see the gag HIV protein in Figure 13). To cater

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for the designed amino acid mutations more than one base was assigned to some positions using the IUPAC DNA codes without exceeding more than three base variations (eight possible combinations) in any group of 27 bases (Figure 12). Where a particular combination of amino acids could not be incorporated, because too many degenerate bases would be required, some or all of the amino acid degeneracy was removed according to the protein consensus design rules outlined above. Also the degenerate codons were checked to determine if they could encode a stop codon, if stop codons could not be avoided then the amino acid degeneracy was also simplified again according to the protein consensus design rules outlined above.

The designed DNA segments were then scrambled randomly and joined to create twenty-two subcassettes approximately 840 bp in size. Extra DNA sequences incorporating sites for one of the cohesive restriction enzymes XbaI, SpeI, AvrII or NheI and 3 additional base pairs (to cater for premature Taq polymerase termination) were then added to each end of each subcassette (Figure 14). Some of these extra DNA sequences also contained, the cohesive restriction sites for SaII or XhoI, Kozak signal sequences and start or stop codons to enable the subcassettes to be joined and expressed either as three large cassettes or one full length protein (Figures 14 and 15).

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In designing the HIV Savine one issue that required investigation was whether such a large DNA molecule would be fully expressed and whether epitopes encoded near the end of the molecule would be efficiently presented to the immune system. The inventors also wished to show that mixing two or more degenerate Savine constructs together could induce T cell responses that recognise mutated sequences. To examine both issues DNA coding for a degenerate murine influenza nucleoprotein CTL epitope, NP365-373, which differs by two amino acids at positions 71 and 72 in influenza strain A/PR/8/34 compared to the A/NT/60/68strain and restricted by H2-Db, was inserted before the last stop codon at the end of the HIV Savine design (Figure 15). An important and unusual characteristic of both of these naturally occurring NP365-373 sequences, which enabled the present inventors to examine the effectiveness of incorporating mutated sequences, is that they generate CTL responses which do not cross react with the alternate sequence (Townsend et. al., 1986). This is an unusual characteristic because epitopes not destroyed by mutation usually induce CTL responses that cross-react.

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Up to ten long oligonucleotides up to 100 bases long and two short amplification oligonucleotides were synthesised to enable construction of each subcassette (Life Technologies). In designing each oligonucleotide the 3' end and in most cases also the 5' end had to be either a 'c' or a 'g' to ensure efficient extension during PCR splicing. The overlap region for each long oligonucleotide was designed to be at least 16 bp with approximately 50% G/C content. Also oligonucleotide overlaps were not placed where degenerate DNA bases coded for degenerate amino acids to avoid splicing difficulties later. Where this was too difficult some degenerate bases were removed according to the protein consensus design rules outlined above and indicated in Figure 12. Figure 16 shows an example of the oligonucleotides design for each subcassette.

Construction of the HIV Savine

Five of each group of ten designed oligonucleotides were spliced together using stepwise asymmetric PCR (Sandhu et al., 1992) and Splicing by Overlap Extension (SOEing) (Figure 17a). Each subcassette was then PCR amplified, cloned into pBluescriptTM II KS⁻ using BamHI/EcoRI and 16 individual clones sequenced. Mutations, deletions and insertions were present in the large majority of the clones for each subcassette, despite acrylamide gel purification of the long oligonucleotides. In order to construct a functional Savine with minimal mutations, two clones for each subcassette with no insertions or deletions and hence a complete open reading frame and with minimal numbers of non-designed mutations, were selected from the sixteen available. The subcassettes were then excised from their plasmids and joined by stepwise PCR-amplified ligation using the polymerase blend ElongaseTM (Life Technology), T4 DNA ligase and the cohesive restriction enzymes Xbal/Spel/Avrll/Nhel, to generate two copies of cassettes A, B and C as outlined in Figure 14 and shown in Figure 17b. Predicted sequences for these cassettes are shown in Figure 30. Each cassette was then reamplified by PCR with Elongase™, cloned into pBluescript™ II KS- and 3 of the resulting plasmid clones sequenced using 12 of the 36 sequencing primers designed to cover the full length construct. Clones with minimal or no further mutations were selected for transfer into plasmids for DNA vaccination or used to make recombinant poxviruses. A summary of the number of designed and non-designed mutations in each Savine construct is presented in Table 1.

TABLE 1

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Summary of mutations

. ,.		Number of mutations			
Construct	No. 225	Designed	Expected in 2 clones	Actual in 2 closes	Non-designed
Cassette A	1896	249	124	107	5 (AC1), 8 (AC2)
Cassette B	1184	260	130	124	11 (BC1), 4 (BC2)
Cassette C	1969	276	138	121	10 (CC1), 14 (CC2)
Full length	5742	785	392	352	26 (FL1), 26 (FL2)

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Summary of the mutations present in the two full-length clones constructed as determined by sequencing. Includes the number of mutations designed, expected and actually present in the 2 clones and the number of non-designed mutations in each cassette and full-length clone.

HIV Savine DNA vaccines and Recombinant Vaccinia viruses

To test the immunological effectiveness of the HIV Savine constructs the cassette sequences were transferred into DNA vaccine and poxvirus vectors. These vectors when used either separately in immunological assays described below or together in a 'prime-boost' protocol which has been shown previously to generate strong T cell responses in vivo (Kent et al., 1997).

DNA Vaccination plasmids were constructed by excising the cassettes from the selected plasmid clones with Xbal/XhoI (cassette A) or Xbal/SalI (cassettes B and C) and ligating them into pDNAVacc cut with Xbal/XhoI to create pDVAC1, pDVAC2, pDVBC1, pDVBC2, pDVCC1, pDVCC2, respectively (Figure 18a). These plasmids were then further modified by cloning into their Xbal site a DNA fragment excised using Xbal/AvrII from pTUMERA2 and encoding a synthetic endoplasmic reticulum (ER) signal sequence from the Adenovirus E1A protein (Persson et al., 1980) (Figure 18a). ER signal sequences have been shown previously to enhance the presentation of both CTL and T helper epitopes in vivo (Ishioka, G.Y., 1999; Thomson et al., 1998). The plasmids pDVERAC1, pDVERBC1, pDVERCC1 andpDVERAC2, pDVERBC2, pDVERCC2 were then mixed

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together to create, plasmid pool 1 and pool 2 respectively. Each plasmid pool collectively encodes one copy of the designed full-length HIV Savine.

Plasmids to generate recombinant Vaccinia viruses which express HIV Savine sequences were constructed by excising the various HIV Savine cassettes from the selected plasmid clones using BamHI/XhoI (cassette A) or BamHI/SaII (cassettes B and C) and cloned into the marker rescue plasmid, pTK7.5, cleaved with BamHI/SalI. These pTK7.5derived plasmids were then used to generate recombinant Vaccinia viruses by marker rescue recombination using established protocols (Boyle et al., 1985) to generate VV-AC1, VV-AC2, VV-BC1, VV-BC2, VV-CC1 and VV-CC2 (Figure 18b).

Two further DNA vaccine plasmids were constructed each encoding a version of the full length HIV Savine (Figure 18c). Briefly, the two versions of cassette B were excised with XhoI and cloned into the corresponding selected plasmid clones containing cassette A sequences that were cut with XhoI/SaII to generate pBSAB1 and pBSAB2 respectively. The joined A/B cassettes in pBSAB1 and pBSAB2 were excised with Xbal/XhoI and cloned into pDVCC1 and pDVCC2, respectively, and cleaved with Xbal/XhoI to generate pDVFL1 and pDVFL2. These were then further modified to contain an ER signal sequence using the same cloning strategy as outlined in figure 18a.

Restimulation of HIV specific lymphocytes from HIV infected patients

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The present inventors examined the capacity of the HIV Savine to restimulate HIV-specific polyclonal CTL responses from HIV-infected patients. PBMCs from three different patients were restimulated in vitro with two HIV Savine Vaccinia virus pools (Pool 1 included VV-AC1 and VV-BC1; Pool 2 included VV-AC2, VV-BC2 and VV-CC2) then used in CTL lysis assays against LCLs infected either with one of the Savine Vaccinia virus pools or Vaccinia viruses which express gag, env or pol. Figure 19 clearly shows, that in all three assays, both HIV Savine viral pools restimulated HIV-specific CTL 25 responses which could recognise targets expressing whole natural HIV antigens and not targets which were uninfected or infected with the control Vaccinia virus. Furthermore, in all three cases, both pools restimulated responses that recognised all three natural HIV antigens. This result suggests that the combined Savine constructs will provide broader immunological coverage than single antigen based vaccine approaches. The level of lysis in each case of targets infected with Savine viral pools was significantly higher than the

lysis recorded for any other infected target. This probably reflects the combined CTL responses to gag, pol, and env plus other HIV antigens not analysed here but whose sequences are also incorporated into the Savine constructs.

CTL recognition of each HIV antigen is largely controlled by each patient's HLA background hence the pattern of CTL lysis for whole HIV antigens is different in each patient. Interestingly, this CTL lysis pattern did not change when the second Savine Vaccinia virus pool was used for CTL restimulation. In these assays, therefore, the inventors were unable to demonstrate clear differences between pools 1 and 2, despite pool 1 lacking a Vaccinia virus expressing cassette CC1 and despite the many amino acid differences between the A and B cassettes in each pool (see table 1).

From the foregoing, the present inventors have developed a novel vaccine/therapeutic strategy. In one embodiment, pathogen or cancer protein sequences are systemically fragmented, reverse translated back into DNA, rearranged randomly then joined back together. The designed synthetic DNA sequence is then constructed using long oligonucleotides and can be transferred into a range of delivery vectors. The vaccine vectors used here were DNA vaccine plasmids and recombinant poxvirus vectors which have been previously shown to elicit strong T cell responses when used together in a 'prime-boost' protocol (Kent et al., 1997). An important advantage of scrambled antigen vaccines or 'Savines' is that the amount of starting sequence information for the design can be easily expanded to include the majority of the protein sequences from a pathogen or for cancer, thereby providing the maximum possible vaccine or therapy coverage for a given population.

An embodiment of the systematic fragmentation approach described herein was based on the size and processing requirements for T cell epitopes and was designed to cause maximal disruption to the structure and function of protein sequences. This fragmentation approach ensures that the maximum possible range of T cell epitopes will be present from any incorporated protein sequence without the protein being functional and able to compromise vaccine safety

Another important advantage of Savines is that consensus protein sequences can be used for their design. This feature is only applicable when the design needs to cater for pathogen or cancer antigens whose sequence varies considerably. HIV is a highly

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mutagenic virus, hence this feature was utilised extensively to design a vaccine which has the potential to cover not only field isolates of HIV but also the major HIV clades involved in the current HIV pandemic. To construct the HIV Savine, one set of long oligonucleotides was synthesised, which included degenerate bases in such a way that 8 constructs are theoretically required for the vaccine to contain all combinations in any stretch of 9 amino acids. The inventors believe that this approach can be improved for the following reasons: 1) While degenerate bases should be theoretically equally represented, in practice some degenerate bases were biased towards one base or the other, leading to a lower than expected frequency of the designed mutations in the two full length HIV Savines which were constructed (see Table 1). 2) Only sequence combinations actually present in the HIV clade consensus sequences are required to get full clade coverage, hence the number of full length constructs needed could be reduced. To reduce the number of constructs however, separate sets of long oligonucleotides would have to be synthesised, significantly increasing the cost, time and effort required to generate a vaccine capable of such considerable vaccine coverage.

A significant problem during the construction of the HIV Savine synthetic DNA sequence was the incorporation of non-designed mutations. The most serious types of mutations were insertions, deletions or those giving rise to stop codons, all of which change the frame of the synthesised sequences and/or caused premature truncation of the Savine proteins. These types of mutation were removed during construction of the HIV Savines by sequencing multiple clones after subcassette and cassette construction and selecting functional clones. The major source of these non-designed mutations was in the long oligonucleotides used for Savine synthesis, despite their gel purification. This problem could be reduced by making the initial subcassettes smaller thereby reducing the possibility of corrupted oligonucleotides being incorporated into each subcassette clone. The second major cause of non-designed mutations was the large number of PCR cycles required for the PCR and ligation-mediated joining of the subcassettes. Including extra sequencing and clone selection steps during the subcassette joining process should help to reduce the frequency of non-designed mutations in future constructs. Finally, another method that could help reduce the frequency of such mutations at all stages is to use resolvase treatment. Resolvases are bacteriophage-encoded endonucleases which recognise disruptions to double stranded DNA and are primarily used by bacteriophages to resolve

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Holliday junctions (Mizuuchi, 1982; Youil et al., 1995). T7 endonuclease I has already been used by the present inventors in synthetic DNA constructions to recognise mutations and cleave corrupted dsDNA to allow gel purification of correct sequences. Cleavage of corrupted sequences occurs because after a simple denaturing and hybridisation step mutated DNA hybridises to correct DNA sequences and results in a mispairing of DNA bases which is able to be recognised by the resolvase. This method resulted in a 50% reduction in the frequency of errors. Further optimisation of this method and the use of a thermostable version of this type of enzyme could further reduce the frequency of errors during long Savine construction.

Two pools of Vaccinia viruses expressing Savine cassettes were both shown to restimulate HIV-specific responses from three different patients infected with B clade HIV viruses. These results provide a clear indication that the HIV Savine should provide broad coverage of the population because each patient had a different HLA pattern yet both pools were able to restimulate HIV-specific CTL responses in all three patients against all three natural HIV proteins tested. Also, both pools were shown to restimulate virtually identical CTL patterns in all three patients. This result was unexpected because some responses should have been lost or gained due to the amino acid differences between the two pools and because Pool 1 is only capable of expressing 2/3 of the full length HIV Savine. There are two suggested reasons why the pattern of CTL lysis was not altered between the two viral pools. Firstly, the sequences in the Savine constructs are nearly all duplicated because the fragment sequences overlap. Hence the loss of a third of the Savine may not have excluded sufficient T cell epitopes for differences to be detected in only three patient samples against only three HIV proteins. Secondly, while mutations often destroy T cell epitopes, if they remain functional, then the CTL they generate frequently can recognise alternate epitope sequences. Taken together this finding indirectly suggests that combining only two Savine constructs may provide robust multiclade coverage. Further experiments are being carried out to directly examine the capacity of the HIV Savine to stimulate CTL generated by different strains of HIV virus. The capacity of the two HIV-1 Savine Vaccinia vector pools to stimulate CD4+ T cell HIV-1 specific responses from infected patients was also tested (Figure 20). Both patients showed significant proliferation of CD4+ T cells although both pools did not show consistent patterns suggesting that the two pools may provide wider vaccine coverage than using either pool independently.

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The present inventors have generated a novel vaccine strategy, which has been used to generate what the inventors believe to be the most effective HIV candidate vaccine to date. The inventors have used this vaccine to immunise naive mice. Figure 21 shows conclusively that the HIV-1 Savine described above can generate a Gag and Nef CTL response in naïve mice. It should be noted, however, that the Nef CTL epitope appeared to exist only in Pool 1 since it was not restimulated by Pool 2. This is further proof of the utility of combining HIV-1 Savine Pool 1 and Pool 2 components together to provide broader vaccine coverage.

The HIV-1 Savine Vaccinia vectors have also been used to restimulate *in vivo*HIV-1 responses in pre-immune *M. nemestrina* monkeys. These experiments (Figure 22) showed, by INF-γ ELISPOT and CD69 expression on both CD4 and CD8 T cells, that the ability of the HIV-1 SAVINE to restimulate HIV-1 specific responses in vivo is equivalent or perhaps better than another HIV-1 candidate vaccine.

This is a generic strategy able to be applied to many other human infections or cancers where T-cell responses are considered to be important for protection or recovery. With this in mind the inventors have begun constructing Savines for melanoma, cervical cancer and Hepatitis C. In the case of melanoma, the majority of the currently identified melanoma antigens have been divided into two groups, one containing antigens associated with melanoma and one containing differentiation antigens from melanocytes, which are often upregulated in melanomas. Two Savine constructs are presently being constructed to cater for these two groups. The reason for making the distinction is that treatment of melanoma might first proceed using the Savine that incorporates fragments of melanoma specific antigens only. If this Savine fails to control some metastases then the less specific Savine containing the melanocyte-specific antigens can then be used. It is important to point out that other cancers also express many of the antigens specific to melanomas e.g., testicular and breast cancers. Hence the melanoma specific Savine may have therapeutic benefits for other cancers.

A small Savine is also being constructed for cervical cancer. This Savine will contain two antigens, E6 and E7, from two strains of human papilloma virus (HPV), HPV-16 and HPV-18, directly linked with causing the majority of cervical cancers worldwide. There is a large number of sequence differences in these two antigens between the two

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strains which would normally require two Savines to be constructed. However since this Savine is small, the antigen fragments from both strains are being scrambled together. While it is normally better for the Savine approach to include all or a majority of the antigens from a virus, in this case only E6 and E7 are expressed during viral latency or in cervical carcinomas. Hence in the interests of simplicity, the rest of the HPV genome will not be included although all HPV antigens would be desirable in a Savine against genital warts.

Two Savines have also been constructed for two strains of hepatitis C, a major cause of liver disease in the world. Hepatitis C is similar to HIV in the requirements for a vaccine or therapeutic. However, the major hepatitis C strains share significantly lower homology, 69-79%, with one another than do the various HIV clades. To cater for this the inventors have decided to construct two separate constructs to cater for the two major strains present in Australia, types 1 aand 3a, which together cause approximately 80-95% of hepatitis C infections in this country. Both constructs will be approximately the same size as the HIV Savine but will be blended together into a single vaccine or therapy.

Overall it is believed that the Savine vaccine strategy is a generic technology likely to be applied to a wide range of human diseases. It is also believed that because it is not necessary to characterise each antigen, this technology will be actively applied to animal vaccines as well where research into vaccines or therapies is often inhibited by the lack of specific reagents, modest research budgets and poor returns on animal vaccines.

EXAMPLE 2

Hepatitis C Savine

Synthetic immunomodulatory molecules have also been designed for treating Hepatitis C. In one example, the algorithm of Figure 25 was applied to a consensus polyprotein sequence of Hepatitis C 1a to facilitate its segmentation into overlapping segments (30 aa segments overlapping by 15 aa), the rearrangement of these segments into a scrambled order and the output of Savine nucleic acid and amino acid sequences, as shown in Figure 26. Exemplary DNA cassettes (A, B and C) are also shown in Figure 26, which contain suitable restriction enzyme sites at their ends to facilitate their joining into a single expressible open reading frame.

EXAMPLE 3

Melanoma Savine

The algorithm of Figure 25 was also applied to melanocyte differentiation antigens (gp100, MART, TRP-1, Tyros, Trp-2, MC1R, MUC1F and MUC1R) and to melanoma specific antigens (BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b and LAGE1), as shown in Figure 27, to provide separate Savine nucleic acid and amino acid sequences for treating or preventing melanoma.

EXAMPLE 4

Resolvase Repair Experiment

A resolvase can be used advantageously to repair errors in polynucleotides. The following procedure outlines resolvase repair of a synthetic 340 bp fragment in which DNA errors were common.

Method

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The 340 bp fragment was PCR amplified and gel purified on a 4% agarose gel. After spin purifying, 10ul of the eluate corresponding to approximately 100 ng was subjected to the resolvase repair treatment. The rest of the DNA sample was stored for later cloning as the untreated control.

2 μL of 10xPCR buffer, 2 μL of 20 mM MgCl₂ and 6 μL of MilliQTM water (MQW) and Taq DNA polymerase were added to the 10 μL DNA sample. The mixture was subjected to the following thermal profile; 95°C for 5min, 65°C for 30min, cooled and held at 37°C. Five μL of 10xT7 endonuclease I buffer, 8 μL of 1/50 μL of T7endoI enzyme stock and 17 μL of MQW were added, mixed and incubated for 30 min. Loading buffer was added to the sample and the sample was electrophoresed on a 4% agarose gel. A faint band corresponding to the full length fragment was excised and subjected to 15 further cycles of PCR. The amplified fragment was agarose gel purified and, along with the untreated DNA sample, cloned into pBluescript. Eleven plasmid clones for each DNA sample were sequenced and the number and type of errors compared (see table)

Buffers were as follows:

10x T7endonuclease buffer

2.5ml 1M TRIS pH7.8, 0.5ml 1M MgCl₂, 25 μ L 1 M DTT, 50 μ L 10mg/mL BSA, 2 mL MQW made up to a total of 5 mL.

5 T7 endonuclease I stock

Concentrated sample of enzyme prepared by, and obtained from, Jeff Babon (St Vincent's Hospital) was diluted 1/50 using the following dilution buffer: 50 μ L 1 M TRIS pH7.8, 0.1 μ L 1M EDTA pH8, 5 μ L 100 mM glutathione, 50 μ L 10mg/mL BSA, 2.3 mL MQW, 2.5 mL glycerol made up to a total of 5 mL.

10 Results

The results are summarised in Tables 2 and 3.

TABLE 2

Total Euros				
Untreated	Resolvase treated			
A/T to $G/C = 6$	A/T to G/C = 1			
G/C to A/T = 12	G/C to $A/T = 7$			
A/T to deletion = 1	A/T to deletion = 1			
G/C to deletion = 6	G/C to deletion = 3			

TABLE 3

Clone summery				
Untreated	Resolvase (realed			
6/11 contained deletions	3/11 contained deletions			
9/11 contained mutations	7/11 contained mutations			

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Clone s	Clone summery			
Untraced	Resolvase treated			
2/11 correct	3/11 correct			

Discussion/Conclusion

While overall the number of correct clones obtained was not significantly different, there was a significant difference in the level of errors. This reduction in errors becomes more significant as greater numbers of long oligonucleotides are joined into the one construct *i.e.*, increasing the difference between untreated *versus* treated samples in the chance of obtaining a correct clone. It is believed that combining another resolvase such as T4 endonuclease VII may further enhance repair or increase the bias against errors.

Importantly, this experiment was not optimised e.g., by using proofreading PCR enzymes or optimised conditions. Finally if the repair reaction is carried out during normal PCR, for example, by including a thermostable resolvase, it is believed that amplification of already damaged long oligonucleotides, and the normal accumulation of PCR induced errors, even using error reading polymerases during PCR, could be reduced significantly. The repair of damaged long oligonucleotides is particularly important for synthesis of long DNA fragment such as in Savines because, while the rate of long oligonucleotide damage is typically <5%, after joining 10 oligonucleotides, the error rate approaches 50%. This is true even using the best proofreading PCR enzymes because these enzymes do not verify the sequence integrity using correct oligonucleotide templates that exist as a significant majority (95%) in a joining reaction.

The disclosure of every patent, patent application, and publication cited herein is incorporated herein by reference in its entirety.

The citation of any reference herein should not be construed as an admission that such reference is available as "Prior Art" to the instant application

Throughout the specification the aim has been to describe the preferred embodiments of the invention without limiting the invention to any one embodiment or specific collection of features. Those of skill in the art will therefore appreciate that, in

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light of the instant disclosure, various modifications and changes can be made in the particular embodiments exemplified without departing from the scope of the present invention. All such modifications and changes are intended to be included within the scope of the appended claims.

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WHAT IS CLAIMED IS:

- 1. A synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide.
- 2. The synthetic polypeptide of claim 1, consisting essentially of different segments of a single parent polypeptide.
- 3. The synthetic polypeptide of claim 1, consisting essentially of different segments of a plurality of different parent polypeptides.
- 4. The synthetic polypeptide of claim 1, wherein the segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to their linkage in said at least one parent polypeptide.
- 5. The synthetic polypeptide of claim 4, wherein the segments in said synthetic polypeptide are randomly rearranged relative to their order or arrangement in said at least one parent polypeptide.
- 6. The synthetic polypeptide of claim 1, wherein the size of an individual segment is at least 4 amino acids.
- 7. The synthetic polypeptide of claim 6, wherein the size of an individual segment is from about 20 to about 60 amino acids.
- 8. The synthetic polypeptide of claim 7, wherein the size of an individual segment is about 30 amino acids.
- 9. The synthetic polypeptide of claim 7, comprising at least 30% of the parent polypeptide sequence.
- 10. The synthetic polypeptide of claim 1, wherein at least one of said segments comprises partial sequence identity or homology to one or more other said segments.
- 11. The synthetic polypeptide of claim 10, wherein the sequence identity or homology is contained at one or both ends of an individual segment.

12. The synthetic polypeptide of claim 11, wherein one or both ends of said segment comprises at least 4 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments.

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- 13. The synthetic polypeptide of claim 10, wherein the size of an individual segment is about twice the size of the sequence that is identical or homologous to the or each other said segment.
- 14. The synthetic polypeptide of claim 13, wherein the size of an individual segment is about 30 amino acids and the size of the sequence that is identical or homologous to the or each other said segment is about 15 amino acids.
- 15. The synthetic polypeptide of claim 1, wherein an optional spacer is interposed between some or all of the segments.
- 16. The synthetic polypeptide of claim 15, wherein the spacer alters proteolytic processing and/or presentation of adjacent segment(s).
- 17. The synthetic polypeptide of claim 16, wherein the spacer comprises at least one neutral amino acid.
- 18. The synthetic polypeptide of claim 16, wherein the spacer comprises at least one alanine residue.
- 19. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is associated with a disease or condition.
- 20. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is selected from a polypeptide of a pathogenic organism, a cancer-associated polypeptide, an autoimmune disease-associated polypeptide, an allergy-associated polypeptide or a variant or derivative of these.
- 21. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is a polypeptide of a virus.
- 22. The synthetic polypeptide of claim 21, wherein the virus is selected from a Human Immunodeficiency Virus (HIV) or a Hepatitis virus.
- 23. The synthetic polypeptide of claim 22, wherein the virus is a Human Immunodeficiency Virus (HIV) and the at least one parent polypeptide is selected from env, gag, pol, vif, vpr, tat, rev, vpu and nef, or a combination thereof.

- 24. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is a cancer-associated polypeptide.
- 25. The synthetic polypeptide of claim 24, wherein the cancer is melanoma.
- 26. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanocyte differentiation antigen.
- 27. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanocyte differentiation antigen selected from gp100, MART, TRP-1, Tyros, TRP2, MC1R, MUC1F, MUC1R or a combination thereof.
- 28. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanoma-specific antigen.
- 29. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanoma-specific antigen selected from BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b, LAGE1 or a combination thereof.
- 30. A synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide.
- 31. A method for producing the synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, said method comprising:
 - linking together in the same reading frame a plurality of nucleic acid sequences encoding different segments of the at least one parent polypeptide to form a synthetic polynucleotide whose sequence encodes said segments linked together in a different relationship relative to their linkage in the at least one parent polypeptide.
- 32. The method of claim 31, further comprising fragmenting the sequence of a respective parent polypeptide into fragments and linking said fragments together in a different relationship relative to their linkage in a respective parent polypeptide sequence.



- 33. The method of claim 32, wherein the fragments are randomly linked together.
- 34. The method of claim 31, further comprising reverse translating the sequence of a respective parent polypeptide or a segment thereof to provide a nucleic acid sequence encoding said parent polypeptide or said segment.

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- 35. The method of claim 34, wherein an amino acid of a respective parent polypeptide sequence is reverse translated to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.
- 36. The method of claim 35, wherein an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.
- 37. The method of claim 35, wherein an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence selected from a palindromic sequence or a duplicated sequence, which is refractory to the execution of a task selected from cloning or sequencing.
- 38. The method of claim 31, further comprising linking a spacer oligonucleotide encoding at least one spacer residue between segment-encoding nucleic acids.
- 39. The method of claim 38, wherein spacer oligonucleotide encodes 2 to 3 spacer residues.
- 40. The method of claim 38 or claim 39, wherein the spacer residue is a neutral amino acid.
- 41. The method of claim 38 or claim 39, wherein the spacer residue is alanine.
- 42. The method of claim 31, further comprising linking in the same reading frame as other segment-containing nucleic acid sequences at least one variant nucleic acid sequence which encodes a variant segment having a homologous but not identical amino acid sequence relative to other encoded segments.

- 43. The method of claim 42, wherein the variant segment comprises conserved and/or non-conserved amino acid differences relative to one or more other encoded segments.
- 44. The method of claim 43, wherein the differences correspond to sequence polymorphisms.
- 45. The method of claim 44, wherein degenerate bases are designed or built in to the at least one variant nucleic acid sequence to give rise to all desired homologous sequences.
- 46. The method of claim 31, further comprising optimising the codon composition of the synthetic polynucleotide such that it is translated efficiently by a host cell.
- 47. A synthetic construct comprising a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said synthetic polynucleotide is operably linked to a regulatory polynucleotide.
- 48. The synthetic construct of claim 47, further including a nucleic acid sequence encoding an immunostimulatory molecule.
- 49. The synthetic construct of claim 48, wherein the immunostimulatory molecule comprises a domain of an invasin protein (Inv).
- 50. The synthetic construct of claim 48, wherein the immunostimulatory molecule comprises the sequence set forth in SEQ ID NO: 1467 or an immune stimulatory homologue thereof.
- 51. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a T cell co-stimulatory molecule.
- 52. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a T cell co-stimulatory molecule selected from a B7 molecule or an ICAM molecule.
- 53. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a B7 molecule or a biologically active fragment thereof, or a variant or derivative of these.

- 54. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a cytokine selected from an interleukin, a lymphokine, tumour necrosis factor or an interferon.
- 55. The synthetic construct of claim 48, wherein the immunostimulatory molecule is an immunomodulatory oligonucleotide.
- 56. An immunopotentiating composition, comprising an immunopotentiating agent selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30 or the synthetic construct of claim 47, together with a pharmaceutically acceptable carrier.
- 57. The composition of claim 56, further comprising an adjuvant.
- 58. A method for modulating an immune response, which response is preferably directed against a pathogen or a cancer, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30, the synthetic construct of claim 47, or the composition of claim 56.
- 59. A method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30, the synthetic construct of claim 47, or the composition of claim 56.
- 60. A computer program product for designing the sequence of a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, said program product comprising:
 - code that receives as input the sequence of said at least one parent polypeptide;
 - code that fragments the sequence of a respective parent polypeptide into fragments;
 - code that links together said fragments in a different relationship relative to their linkage in said parent polypeptide sequence; and

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- a computer readable medium that stores the codes.
- 61. The computer program product of claim 60, further comprising code that randomly rearranges said fragments.
- 62. The computer program product of claim 60, further comprising code that links the sequence of a spacer residue to the sequence of said at least one parent polypeptide or to said fragments.
- 63. A computer program product for designing the sequence of a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, comprising:
 - code that receives as input the sequence of at least one parent polypeptide;
 - code that fragments the sequence of a respective parent polypeptide into fragments;
 - code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment;
 - code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence; and
 - a computer readable medium that stores the codes.
- 64. The computer program product of claim 63, further comprising code that randomly rearranges said nucleic acid sequences.
- 65. The computer program product of claim 64, further comprising code that reverse translates an amino acid of a respective parent polypeptide sequence to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.
- 66. The computer program product of claim 63, further comprising code that reverse translates an amino acid of a respective parent polypeptide sequence to provide a codon



which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.

- 67. The computer program product of claim 63, further comprising code that links a spacer oligonucleotide to one or more of said nucleic acid sequences.
- 68. A computer for designing the sequence of a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said computer comprises:
 - (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
 - (b) a working memory for storing instructions for processing said machine-readable data;
 - (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polypeptide sequence; and
 - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence.
- 69. The computer of claim 68, wherein the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking together said fragments in a different relationship relative to their linkage in the sequence of said parent polypeptide.
- 70. The computer of claim 68, wherein the processing of said machine readable data comprises randomly rearranging said fragments.
- 71. The computer of claim 68, wherein the processing of said machine readable data comprises linking the sequence of a spacer residue to the sequence of said at least one parent polypeptide or to said fragments.

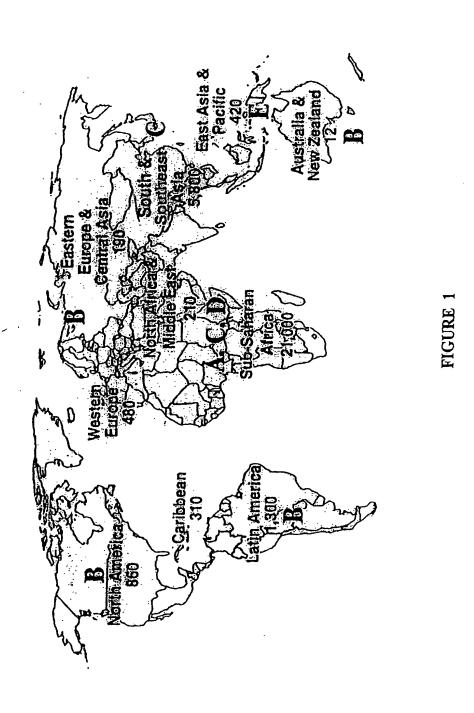
- 72. A computer for designing the sequence of a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said computer comprises:
 - (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
 - (b) a working memory for storing instructions for processing said machine-readable data;
 - (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polynucleotide sequence; and
 - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polynucleotide sequence.
- 73. The computer of claim 72, wherein the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments, reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment and linking together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence.
- 74. The computer of claim 72, wherein the processing of said machine readable data comprises randomly rearranging said nucleic acid sequences.
- 75. The computer of claim 72, wherein the processing of said machine readable data comprises reverse translating an amino acid of a respective parent polypeptide sequence to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.

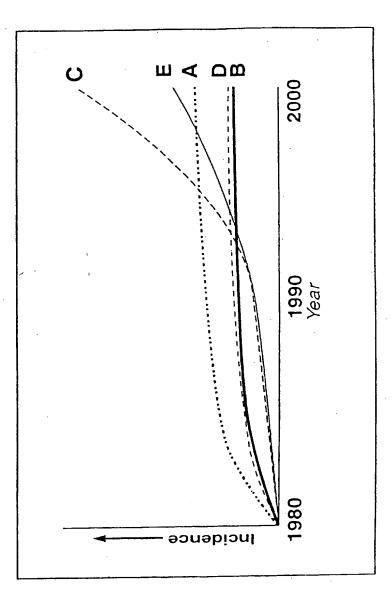
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76. The computer of claim 72, wherein the processing of said machine readable data comprises reverse translating an amino acid of a respective parent polypeptide sequence to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.

77. The computer of claim 72, wherein the processing of said machine readable data comprises linking a spacer oligonucleotide to one or more of said nucleic acid sequences.

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/<-
                                                                      nls
                                         membrane binding
   DESIGNED SEO MGARASVLSGGKLDAWEKIRLRPGGKKKYKMKHLVWASRELERFALNPGLLETAEGCQQILEQLQSALKT
                                                                                                                        s
   MUTATED AAS
                          mgarasvlsggkldawekirlrpggkkkykmkhlvwasrelerfalnpglletaegcoolieolostlkt
   E-ISOLATE
  70
                                                                                                                                                                    69
                                                                                                                                                                    6 B
                                                                                                                                                                    70
                                                                                                                                                                    62
                                                                                           /<- nls ->/
  DESIGNED SEQ GSEELKSLYNTIATLMCVHORIEVKDTKEALDKIEEEOKKSQQK.....TQQAAA..DT.GS...SSKV
  MUTATED AAS
                         GSEELKSLYNTIATLWCVHQRIEVKDTKEALDKIEEVQKKSQOKK.....QQAAA..DT.GS...SSKV
  E-ISOLATE
126
                                                                                                                                                                 120
                                                                                                                                                                 125
                                                                                                                                                                 123
                                                                                                                                                                 110
                                                                                                                                                                106
                                                                                                                                                                 106
                               p17 \/ p24
 DESIGNED SEQ ....SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH
 MUTATED AAS
                                                                                             ΑS
                        . \dots \texttt{SQNYPIVQNAQGQMVHOPLSPRTLNAWVKVIEE} KGFNPEVIPMFSALSEGATPODLNMMLNIVGGHAMMAN STANDARD ST
 E-ISOLATE
                         ????SqNYPIVQNaqqQm?hQ?lSPrTLnAwVKviEekaFspEVIPmFsaLSEGATpQdLNmMLNiVqGH
 CONSENSUS - A
                                                                                                                                                               194
 CONSENSUS - B
                                                                                                                                                               185
 CONSENSUS - C
                         191
 CONSENSUS-D
                          ....-T----T----T
                                                                                                                                                               188
 CONSENSUS-F
                         CONSENSUS-G
                                                                                                                                                               170
 CONSENSUS-H
                         CONSENSUS-O
 CONSENSUS-CP2 ----??---???----??-----?V---?-?-?--?-?-?-?-?-----?-?-?-?--
DESIGNED SEQ QAAMQMLKETINEEAAEWDRVHPVHAGPIPPGOMREPRGSDIAGTTSTLQEQIGWMTN...NPPIPVGDI
MUTATED AAS
                       QAAMOMLKETINEEAAEWDRVHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQIGWMTN...NPPIPVGDI
E-ISOLATE
                         QAAMQMLKdtINeEAAewDr?HPVhAgPippgQmREPrGSDIAGtTStlqEqigwmTs...NPPiPVGdI
CONSENSUS - A
                                                                                                                                                               261
CONSENSUS-B
                                                                                                                                                               251
                        -G-L-V-EV---?--T--P??-L---I--T---Q---?-T-R.??-??
                                                                                                                                                               257
CONSENSUS-D
                                                                                                                                                               255
CONSENSUS - F
                                                                                                                                                               239
CONSENSUS-G
                                                                                                                                                              233
CONSENSUS-H
CONSENSUS-O
```

FIGURE 3

MHR

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								Zn-mot	if
			p24 \/	V	'p2'	\/ p7		/<	
	SILKALGTGATLEEMMT	» cocyconeus	/አርህ፣.ልፑልክ	4021	TH AN	TMMORGN	F. KGOKRIT	KCFN	
DESIGNED SEQ MUTATED AAS	T R P S	G G	CAR V DALEZA	v	NN		RP V	,	
ISOLATE-E	SILKALGTGATLEEMMT	ACQGVGGPSHK	arvlaean	ISQA	QH.AN	. IMMORGNI	F. KGQTR. I	KCFN	
CONSENSUS-A	sILraLg?gAtLeEMM	rac0qVqqPgH	KATVLAEA	mSqv	.q???n?	?.iMmQrGr	f rgqkr?	ikcfn	38
CONSENSUS-B	m v -Da				.tn-s.a	t?	n-rkc	V	39
CONSENSUS-C	m D - C			a	. nn	8-	K-p1	v	38
CONSENSUS-D	tKP?	s-		a	.tn.s-ta	a	K-prki		39
CONSENSUS-F	TKP			a	.TN?a	KS-	KR-1	y	38: 36:
CONSENSUS-G	T?P	? - :		A	.SGA-/	4.?K??	- K-P??-	2	35:
CONSENSUS-H	??SI\ OK?P?\	?	?		IN : A-	. VE	N D2D.C.		358
CONSENSUS-O CONSENSUS-CP2		?		- ? ? ? ? ? ? .	?Q?	VF?-?-?	G??-?	?	262
			1	cds ->					
	Zn-motif ->/	/<-Zn-moti		p7·\/		1'	// be		
	CGKEGHLARNCRAPRKKG	CWKCGKEGHON	KDCTE.	ROANFL	GKIWPSN	KG . RPGNF	PQSKP		
MUTATED AAs	I K	R			s	н	L R		
ISOLATE-E	CGKEGHLARNCRAPRKKG				GKIWPSN				
CONSENSUS-A	CGkEGH1ArNCrAPrKk	GCwKCakEGHQ	mKdCT.?e	.rQANF	lgkiwpS	sKG.RPgNI	PpQsRp		443
CONSENSUS-B	· · · · · · · · · · · · · · · · · · ·			7		h	-1	2717	453
CONSENSUS-C	÷					?	·L???	????	439
CONSENSUS - D	i-k					h	.1		449
CONSENSUS-F	i-k	r				n	. D	• • • •	445 414
CONSENSUS-G	?	?				7	7		406
CONSENSUS-H	??-		2 N	·	V D(2GTY	V-???		411
CONSENSUS-0	I-?KR		:N	2221	22-7	??-?	V-?????.		306
CONSENSUS-CPZ	?Кк-	кО							- , ,
	vpr binding					ν	pr bindi:	ng j	p6
	•							term	inus
	/<>/	\	/ (minor		(min	or) \/	/<>/	/	(80%)
DESIGNED SEQ MUTATED AAs	EPTAPPAE	NF.GFGE	ETT.PS		ЭК О Р	KEHYPPSAS L L	CLKSLFGND	PLSQ S	
ISOLATE-E .	EPTAPPAE	NW.GMGE	E		וסאנ	KEHPPPSVS	LKSLFGNDI	PLSQ	
CONSENSUS-A	EPtAPpAE	?f?gmge	eit.s?	pkge	gkd??	ke??ppl?	slKSlFGNI	plsQ .	485
CONSENSUS-B	?????~e								500
CONSENSUS-C	??????????								479
CONSENSUS-D	· · · · · · · · · · ·								495
CONSENSUS-F									482
CONSENSUS-G	?								440
CONSENSUS-H									436
CONSENSUS - O	?-SM	· · · · · · · · · · · · · · · ·	2VK. ?Q	EN-?	G	:-LYFA	T-	UŞ	444
CONSENSUS-CP2	II-	1.::0-	- r K . ?	? - ??	ff?	2.2P======	?-	17	333

CONSENSUS A-CPZ FROM LOS ALAMOS HIV SEQUENCE DATABASE ISOLATE-E SEQ FROM ISOLATE 93TH253 THAILAND

Underlined AA are not present in all overlapping segments

FIGURE 3 (Cont)

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DESIGNED SEQ	FFRE.NLAFOOGKAREF. P E	SSE.	.OTGANSSASRKLGDO R PT	GGGAI	ERQ O
ISOLATE-E	FFRE.NLAFQOGKAREF.	sse.	.QTGANSSASRKLGDO	GGAI	CRQ
CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U CONSENSUS-CP2	FFRE.NLAFQQGEAR?Fdpket	?????????? 	Rap-r-E-qV RAP-TQV. RAPE-RV TS-PI-P-?	W-T-NNS-5:::-EA-A RGSNT.FSEAGAE W-TNP-SeT-A GSEGT-ES?- W-G-K.T-SET-A	CR 41 G?? 35
	protease \/	<- gag cds	end		
DESIGNED SEO MUTATED AAS	GTSSSFSFPQITLWQRI	V I	LDTGADDTVLEDINLP EM	GKWKPKMIGGIGGFIKV R	RQYD
ISOLATE-E	GTSSSFSFPQITLWQRF	PLVTIKI GGQLKEALI	DTGADDTVLEDINLP	CKMK ÞKMIGGIGGFIKVI	ROYD
CONSENSUS-A	G???SF?FPQITLWQR	PLVTV?I?GQLIEAL	LDTGADDTVLEDINL	GKWKPK?IGGIGGFIK\	VROYD 96
CONSENSUS-D CONSENSUS-O	tVs	IK-GK IK-GK -IA-VG-H-C-?-	E	M	115 KE-? 94
MUTATED AAS	OILIEICGKKAIGTVLVGP	TPVNIIGRNMLTQIG L L	R E	LKPGMDGPKVKQWPLTE	
ISOLATE-E	OIFIEICCKKYICLAFAC	tpvni i grnmltqi g	CTLNFP1SP1DTVPVK	LKPGMDGPKVKQWPLTE	EKI ·
CONSENSUS-D CONSENSUS-O	Ollieicgkk?igtvLvgi	LL LL ?IGL-	RAP	G	7 184 7 189
	L MAST.	D67N	I I K70R		
DESIGNED SEQ P MUTATED AAS	ALTEICKEMEEEGKISKIC	;penpyntpvfaikk) I	(DSTKWRKLVDFRELM	KK I OD P WE V OLGS I PREAK	MA
SOLATE-E F	O ALTEICKEMEÉEGKISKIG	PENPYNTPVFAIKKK	DSTKWRKLVDFRELNI	KRTODFWEVQLGI PHPAC	;LK
CONSENSUS-A	KALT?IC?EMEKEGKISKI VETR	GPENPYNTPVFAIKK	KDSTKWRKLVDFREL	KRTODFWEVOLGIPH?A	AGLK 231
CONSENSUS-D CONSENSUS-O	ETR- EAQQR- EKDL ??E??-?-??-	I I	?N	?PG	227 255
	KKSVTVLDVGDAYFSVPLD	ESFRKYTAFTIPSIN KD T			
SOLATE-E K	K KS VTV LDV GD AYFSVP L D	G ESFRKYTAFTIPSIN	NETPG1RYQYNVLPQ0	WKGSPAIFQSSMTKILE	PF
ONSÉNSUS-B	KKKSVTVLDVGDAYFSVPL	-kd]	PSPQ	
ONSENSUS-D	0?0	-eDV- -PDV-		AS	D 295 325

polymerase motif

FAGURE 4

DESIGNED SEQ MUTATED AAS	V E P R A E T A	
ISOLATE-E	Q QP1ELPEKDSWTVNDIQKLVGKLNWASQIYAGIKVKQLCKLLRGTKALTDIVPLTEEAELELEENREI	
CONSENSUS-A	QP??LPEXDSWTVNDIQKLVGKLNWASQIYAGIK?KQLC?LLRGAXALTDIV?LTEEAELELAENREI	42 46
CONSENSUS - B		
ISOLATE-C		46
CONSENSUS - D	-SIKE	41
CONSENSUS-O		46
CONSENSUS-CP	IOD-E??????-??????	32
CONSCINSCO		
DESIGNED SEQ MUTATED AAS	LREPVHGVYYDPSKDLVAEVOKOGODOWTYQIYOEPFKNLKTGKYSRKRSAHTNDVRQLTEVVOKIATE K I \overline{I} G F F(error) A M G K AA \underline{V}	
ISOLATE-E	.LRIPVHGVYYDPSKDLVAEVQKQGQDQWTYQIYQEPFKNLKTGKYSRKRSAHTNDVRQLTEVVQKIATE	
CONSENSUS-A	.LK?PVHGVYYDP?KDLVAE?QKQGQDQWTYQIYQEPFKNLKTGKYA?KRSAHTNDVKQLTEVVQKV??E	484
CONSENSUS-B		533
ISOLATE-C		531
CONSENSUS-D		479
CONSENSUS-O		532
CONSENSUS -U	ES11	367
CONSENSOS-CP2		
•	p51 \/	
DESIGNED SEO	SIVINGKTPKFRLPIQRETWETWWMEYWQATWIPEWEFVNTPPLVXLWYQLEKDPIVGAETFYVDGAASR	
MUTATED AAS	K K A TD E AV N	
NOTHI DE 12-		
ISOLATE-E	SIVIWGKTPKFRLPIQRETWETWWMEYWQATWIPEWEFVNTPPLVKLWYQLEKDPIVGAETFYVDGAASR	550
CONSENSUS-A	SIVIWGK?PKFRLPIQ?ETWE?WWMEYWQATWIPEWEFVNTPPLVKLWYQLEKDPI?GAETFYVDGAANR	602
CONSENSUS-B		. 002
ISOLATE-C		600
CONSENSUS-D		
CONSENSUS - O		541
		602
CONSENSUS-CPZ	????????????????????	416
DESIGNED SEO	ETKLGKAGYVTDRGROKVISLTETTNOKTELHAIHLALQDSGSEVNIVTDSQYALGIIQAQPDRSESEVV	
MUTATED AAS	IN D O O T T K T	
	ETKLGKAGYVTDRGRQKVISLTETTNQKTELHAIHLALQDSGSEVNIVTDSQYALGIIQAQPDRSESEVV	
ISOLATE-E		
	ETK?GKAGYVTDRGRQKVVSLTETTNOKTELHAIHLALODSGSEVNIVTDSQYALGIIQAQPDRSESE?V	618
CONSENSUS-A	`	672
CONSENSUS-B		
	L	670
CONSENSUS-D	L	602
CONSENSUS-O	?LEQ-K-?IIK-?A-M-?L?KE???-SSTQ-?-PI-	672
CONSENSUS - U		459
CONSENSUS-CPZ	????-???????-??QA?-?L?????????L-	
	TO THE PROPERTY OF THE PROPERT	
DESIGNED SEQ	SQIIEELIKKEKVYLSWVPAHKGIGGNEQVDKLVISGIRKVLFLDGINKAQEEHERYHSNWRTMASDFNL SA D K NE	
MUTATED AAS	N K R A SA D K NE	
	Q SQIIEELIKKEKVYLSWVPAHKGIGGNEQVDKLVISGIRKVLFLDGINKAQEEHERYHSNWRTMASDFNL	
ISOLATE-E		
	NQIIEKLI?K?KVYLSWVPAHKGIGGNEQVDKLVS?GIRKVLFLDGIDKAQE?HE?YH?NW?AMASDFNL	681
CONSENSUS - A		742
CONSENSUS-B		
ISOLATE-C		740
CONSENSUS-D		669
CONSENSUS - O		742
CONSENSUS-U		510
CONSENSUS - CPZ	QQ-D??????	
	TO SOLVE TO SOLVE UN VIDENCE OF THE PROPERTY OF THE	
DESIGNED SEO	PPIVAKEIVANCDKCOLKGEAMHGOVDCS PGIWOLDCTHLEGKVILVAVHVASGYIEAEVI PAETGOETA	
MUTATED AAS	p s I N I	
•	С	

FIGURE 4 (Cont).

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```
ISOLATE-C
                                                     880
CONSENSUS-D
                                                      798
CONSENSUS-O
CONSENSUS-U
DESIGNED SEQ AEHLKTAVOMAVFIHNFKRKGGIGGYSAGERIIDIIATDIOTKELOKOITKIONFRVYYRDSRDPIWKGP
MUTATED AAS
        {\tt AEHLKTAVQMAVFIHNFKRKGGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYYRDSRDPIWKGP}
ISOLATE-E
        AEHLKTAVQMAVFIHNFKRKGGIGGYSAGERIIDIIA?DIQTKELQKQI?KIQNFRVYYRDSRDPIWKGP
CONSENSUS-A
        CONSENSUS-B
ISOLATE-C
CONSENSUS-D
                                                     865
CONSENSUS-O
CONSENSUS-U
vif cds ->
DESIGNED SEQ AKLLWKGEGAVVIODNSDIKVVPRRKAKIIRDYGKQMAGDDCVAGRQDED
MUTATED AAS
       AKLLWKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMAGDDCVAGRQDED
ISOLATE-E
       AKLLWKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMAGDDC?AGRQDED
CONSENSUS-A
       CONSENSUS-B
ISOLATE-C
                                                    1000
CONSENSUS-D
                                                    925
CONSENSUS-O
                                                    1008
742
```

CONSENSUS A-CPZ FROM LOS ALAMOS HIV SEQUENCE DATABASE ISOLATE-C FROM GENBANK U46016 HIV-1 SUBTYPE C (ETHIOPIA) ISOLATE-E FROM GENBANK U51189 HIV-1 SUBTYPE E ISOLATE 93TH253 (THAILAND)

<- pol cds

DESIGNED SEQ		104710401	mpMp1	PRWTG	Т.37КННМ	YISKK	AKGWF	ҮКННҮ	ESQH!	PKVSSE	AHI PI'GE	Ан	(PAT	
DESIGNED SEQ MUTATED AAS	•	L.	К	K		п								
ISOLATE-E	MENRW.Q													
		.VMIVWO					r s b CWI	CVBHH	FESR	hkvsS	EVHI PLG	d A	RLVV	6
CONSENSUS-A	MENRW.		VDRMI	IRTWN	PLAKHH	MIVON	CAKGA		Yt-	-ri			i	6
CONSENSUS-B														
ISOLATE-C	MENRW Q	VLIVWOV	/DRMKI	RTWNS	PAKHUM	HISKN	2D		rd-p-	I		E		65
CONSENSUS-D														54
CONSENSUS-O CONSENSUS-CP2	2 -????.?	??	-	-??-?-	?-:	[???-	2227-	, ,		• • • •				34
DESIGNED SEQ				T TUDO!	ייייייייייייייייייייייייייייייייייייייי	meni.	T.TOTA	LOYFT	OCFSE	STIRR	AILGQIV	RRRC	EYP	
DESIGNED SEQ	RTYWGLQT	LCE KOM ÖT	GHGVS	T EMKÖI	CKISIU	OPPD	н	<u>¥</u>	A	A	HR :	S	Q	
MUTATED AAs	к н	я н	O	K	5	•	==	Y						
	- 1							-						
•	RTYWGLQ		cucus	TEWBOI	CRYSTO	DPDL	ADOLIF	ILQYFI	OCFSE	STIRR	AT FEGAN	RRC	EYP	
ISOLATE - E														
	Designation 1	TGETDWH	r.GhGV	SIEWro	KRYST	VDPDI	ADgLI	HLhYF	dCFS	dsair	AllGei\	/RPR	CEYO	136
CONSENSUS-A	RITMGLA	TGETDWH	0	k				y		e	h	s		136
CONSENSUS-B	KTYWGLOT	CERDWHI	GHGVS	IEWRLE	SYNTO	/DPGL	ADHLI1	IMHYFT	CFAE	SAIRK	ILGYRV:	SPRCI	DAG	132
ISOLATE-C CONSENSUS-D	k	?	0	K	JR	G	. -	- MY		E?	n	5 /		118
CONSENSUS-0	k	P?E-		?Y	-?-K	1 E7	rRM-		TT	??	QR-	DIK.	:	76
CONSENSUS-CP2		33		??	G?-?	. ?1	[<u>-</u> ??-	-??	??	33-3-3			· ! - K	,,
CONSENSOS-CFA		•											•	
						vpr	cds -	>						
								n	TVCU	DENITA	MCH			
DESIGNED SEQ	SCHNKVGS	LOYLAL.	KAL	. ITPKK	IRPPLE	SVKK	TEDEN	E	T R	G	2 •0.,			
UTATED AAS	A		T	ĸ	K		K	E	1 ^	•				
								B11/DAV	T WOL	DENDT	NGHS			
ISOLATE-E	SGHNKVGS	LOYLAL.	KAL	. TTPKR	IRPPLE	SVKKI	, I EDKW	MAPON						
						DO1- W	T & PDD	Nganu	KTRG	HRGSR?	mNgH\$			191
CONSENSUS-A	AGHNKVG	SLQYLAL	.kAL.	VaPt	KAKPPL	PSVK	Trenk	K	K-	ht				191
		SLOYLAL	.a	1t-k	-1		VEDEM	いいとりひん	TRGR	RGNHTN	NGH			
SOLATE-C		LOYLAL												186
ONSENSUS-D	?		. t	iK	-1	K-		K22	7 T - D	OT.2 - 2.5				161
	?\$0	T?	.?-V.	K??	??	03		K::	D222	- 2EN2T	R			107
		2 2 - 2	7-7-7	つつつつつつ	77R77?	???		n::						

÷ .	/<-	.01	<- v igomeriz	if cds ation	-	>/		LR domain	
DESIGNED SEC	MEO.	AP EDQGPQREPY	NEWALELL	EELKQEAV		regāi ae.			
MUTATED AAs		SS	T	н	G	H	E	I	
ISOLATE-E	MEQ A	AP EDQGPQREPYI	NEWALELL	N EELKQEAVI	RHFPRPWLHNI	LGQYIYET	rygdtwsgvea	LIRTLQQL	
CONSENSUS-A	MES	AP.EDQGPQREP	??E??LELI	LEELKHE?V	RHFPR?WLHG	LGOHIY?	TYGDTWEGV?	Alirilool	58
CONSENSUS-B	q??	?	N-Wt	?-A-	i?	'E	E		65
ISOLATE-C	MEO A	P EDOSSOREPYN	NEWTLELL	EELKNEAVF	RHFPRPWLHGI	GQYIYN N	iygdtwegvea	IIRILQQL	
CONSENSUS-D	Q	Y	N-Wt	S-A-	IS	?E	E	-?	64
CONSENSUS-0	Q	naf	N-Wt	?-A-	pa	yE	m		66
CONSENSUS-U	Q	AH	N-WT	Q-A-	s	E	E	S	67
CONSENSUS-CP	zQ	,?-??	WT-	?-N-A-	?P?-??	??-???-	?-???????-	??????-??	33
	L	R domain ->/	tat cds	: ->					
DESIGNED SEO	MFIH F	RIGCOHSRIGIL	RORRA	RNGASRS					
MUTATED AAS	LV	R I	G.	S					
ISOLATE-E	MFIH F	RIGCOHSRIGIL	RORRA	RNGASRS				•	
CONSENSUS-A	LF?H.F	RIGCOHSRIGII	?GRRG	.RNGA?RS\$	\$				84
CONSENSUS - B	i-?-	rt	g a	?S					93
ISOLATE-C	LFVH FF	RIGCOHSRIGIF	AREKRO	EWSW					
CONSENSUS-D		t .							93
CONSENSUS-0	ty	, ? ?	???-rg:	rss					94
CONSENSUS-U		T.							96
CONSENSUS - CPZ	??I?	???-??L.	PQR	. S SN					54
		-						•	

	intramolecular 3'sj 3'sj disulfide bonding \/ \/ rev cds ->/<- nls ->/							
MUTATED AAS	MDPVDPNLEPWNHPGSQPTTACSKCYCKKCCFHCQLCFLKKGLGISHGRKKR KQRRGAPQSRKDHQYP R K K T Y Y T R R SE Q MELVDPNLEPWNHPGSQPTTACSKCYCK*CCWHCQLCFLKKGLGISHGRKKR KHRRGTPOSRKDHQYP M**PVDPNLEPWNHPGSQPTTACSKCYCK*CCWHCQlCFLKKGLGISYGKKR: r**RRgtPOS*RDHQYP	64 68 65 66 68 55 68 45						
· e:	xon \/ exon							
MUTATED AAS	IPEQPLPQTRGGNPTDPKESKKEVASKTETDPCD S S P D G E K E A F IPEQPLPIIRGGNPTDPKESKKEVASKAETDPCD							
CONSENSUS - A CONSENSUS - B CONSENSUS - C CONSENSUS - D CONSENSUS - F CONSENSUS - O CONSENSUS - U	ipKQplPqtgg??ptgpkESkKkVeSKteTDrf?\$ Ls?s-pr-D	95 99 98 99 96 83 101						

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			high-affinity binding site nls							
	\/ 3' sj	exon \/ 6	exon /<-	->/ ⁻						
DESIGNED SEC	MAGREGETDE ELL	RAVRIINI LYQSNPYF	SSEG TROTRKNRA	RRWRARQRQIRAI	SERI LSTCLGRS					
MUTATED AAs	D N	кі к	SAR	E .HS	W NF P					
ISOLATE-E	MAGRSGSTDE ELL	RAVRI INI LYQSNPYP	SSEGGTROTRKNRR	RRWRARQRQIRAIS	SERILSTCLGRS					
CONSENSUS - A	MAgRSG?sDE.eLL	.KAIRIIKILYQSNPy	PkPkg.srqarknr	rrrwrarqrqids1	SeRILStCLGRP	66				
CONSENSUS-B		tV-1fp				67				
ISOLATE-C		KAVRIIKILYOSNPYP								
CONSENSUS-F		. R-?-Y				61				
CONSENSUS-O		?QQ?				56				
CONSENSUS - U		. RVV				67				
CONSENSUS-CP	Z?E-??????-:	??-VK?	·?-??-?R-?·	???-????	??-V-?-??	41				
	Leu-rio		•							
	effector o									
	/<	·>/		•						
ESIGNED SEQ	AEPVPLQLPPLERLHI	DCSEDCGTSGTQQSQG	TETGVGRPQISGES	SVILGPGTKN						
UTATED AAs	И	SD	<u>N</u> L	AV S						
SOLATE-E	TEPVPLQLPPLERLHL	DCSEDCGTSGTQQSQG	TETGVGRPQI SGES	SVILGPGTKN						
ONSENSUS - A		LDCsEdcgTSgTQq?q			•	120				
ONSENSUS - B		?				115				
SOLATE-C	AEPVPLQLPPLERLNL				,					
ONSENSUS - F	E??	IN??-E.Q-A?E	ST-G-	-нE\$		105				
ONSENSUS-O		IRDP-?D?L????TVDI				95				
ONSENSUS-U	IC	P	TS-PI-G-	TIE\$		123				

							pho	5	ph	os
DESIGNED SEO MTPL MUTATED AAs		L	VF	<u>K</u>	К	K	IKRTRERA E I			
CONSENSUS-A mtPL???	• • • • • • • • • • • • • • • • • • • •	~ :	f -	? r-	i - R	?	a	·		57 56
ISOLATE-C MVDLLA		ALI I A I VVI	IYAIT	EYRK	PPKÖK	KIDKL	-d	. 7		57
CONSENSUS-D -Q	v-lA-v- LAIS?TA	<u>i</u>	I-	crr	-KF	N	YE??	·	- 	51
CONSENSUS-F -S??	LAIS?TA	1	2 62	יכם ז	v - 2 - 220ī	DR?E?E-LER	.LR?-IR	.DD)Y	42
CONSENSUS-O -H??		T >	CV-	R-	TRK		.LD	·		57
CONSENSUS-U -0 CONSENSUS-CPZ??	7;???L?????	???W?-CI?	??1??	??-??	YK???	??????-?	.??I?????	. ????	??-	14
DESIGNED SEQ EGDTEE I	STM VDM G	NYDLGVDNN	IL.							
MUTATED AAS. R	AL									
200775	L?kLVEM.C	nvalavan	NLS							78
CONCENCIIS -B e Ge-	-sa-?????-	H?apwdvd	D							79
	STM VDM G	いとといるとい	-dm- 							80
	-saG	DETR-DIT?								73
	-A?G VM???SH-	FONDM FE	??							59
	-ST+M	YEYILDND								81
CONSENSUS-U DE		EVMDS 33	SODE							23

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<- vpU cds signal peptide / gpl20

					•		•	
	•							
	DESIGNED SEC	O MRVKETO	MUMBAIT AK				VTVYYGVPVWRDADTTLFCAS	
	MUTATED AAS		R	м	M M	E	ET	
	CONSENSUS - A						WtVyYGVPVWkdaeTTLfcAS	
	CONSENSUS - B	??k	rkh-???	??1	m1m	. s	e-t	
	CONSENSUS - C	r	?r-w-gwi	I <i>L</i> G	Fwmlm	vg.n	<u>e</u> -k	53
	CONSENSUS - D						E-t	52
	CONSENSUS - E	Ket	-m-wpnk	1-	lv3	sSd .N	rd	55
	CONSENSUS - F	-?-R-M	-R-W-HGK	LLF	iL	n	e-T	53
	CONSENSUS - G	-?-k	-r-W-Hk	L-	LV	ssn.n	ED	54
	CONSENSUS - O	-t-tMKa	aM?KrNr.Kl	?lylar	nALi-P	LS??Q-Y	ASE?Pv	51
	CONSENSUS-U	-?-?E?-	-R-??-??	???	?	???-?-		36
	CONSENSUS - CP	Z -??????	?-???-?.???	??????	-????.	?T??	???-?P??	19
			*		^^^		•	
			•					
,	DESIGNED SEQ	DAKAHETEVE	INVW ATHACVPTDP		VTENFNM		DEDVISLWD QSLKPCVKLT	
/	MUTATED AAS	YD		vv		D D	HI	
	CONSENSUS - A	dAkAydtE?	HNVW?aTHaCVPTD	PnPqEi?le.	NVTE?Fn:	πwkΝπΜVeΟι	nheDiiSLWD.qSLkPCvkLt	113
	CONSENSUS-B							119
	CONSENSUS - C	e?-v		mv	n	dd		119
	CONSENSUS - D	s-k?-a	i		N			117
	CONSENSUS - E						qv?	121
	CONSENSUS - F						-T	120
	CONSENSUS-G				n		E	120
	CONSENSUS - O	NLTSq	IsQ	?-?-yp-?.	d1	Yd	дМ-	114
	CONSENSUS - U						,?	91
	CONSENSUS-CP2	?-???\$????	?-??V?	-????	????-	????-???	56
		• •					•	
	DESIGNED SEQ MUTATED AAs	PLCVTLNCTN	anlinun h	YPERVARIAE	BLE REGI	ONS 1/2	:	•
							-	
	CONSENSUS-A	PLCVTL?C . ?	'??????????n?t?	?????????n	3633333	renerere.	????????m	126
	CONSENSUS-B						????????	133 132
	CONSENSUS - C							
	CONSENSUS - D						???????????	131 150
	CONSENSUS-E						????? ?tLkE	139
	CONSENSUS - F						ennNstv???	143
	CONSENSUS-G							129
	ONSENSUS-O	rQmic		1		· · · · · · · · · · · ·		105
	CONSENSUS-U			3.	. ?		P???????	60
	ONSENSUS-CPZ	-:-:::			-:	· · · · · · · · · · ·		30
			*** ***					
	ESIGNED SEO	บ	YPERVARIABLE RE	egrons 1/2				
	UTATED AAS	••		•,				
• •	DINIED AND							
_	ONSENSUS-A	2 26	ikNCsfNmTtelrdk	kakvvslfYr	1 DvVai?	???????n?	?????n??????????	160
	ONSENSUS-B	P770-77777	isi	ve-ak	b-a	?-	?????	169
	ONSENSUS-C	-7	a?	A	i-pl-		ss	166
	ONSENSUS-D						t	165
	ONSENSUS-E	- a- v		hak	i		s??	185
	ONSENSUS-E	ep ca		O? Ha	I-p-s	n	s??	177
	ONSENSUS-F	- A- *	ni	-krE-1	n-n	?s	ssd	182
_							rm	164
	ONSENSUS-O			-k+2-a	D-n	n		137
C	ONSENSUS-U						T	73
C	ONSENSUS-CP2	-::-:						
				•	•	. AAA	•	
	e,	-	-					
		TO 7 T NICTOTE 1/7 L	(0) CDKUSENDI DI U	YCAPAGVATI	KCMDKME	NGTGPCKNV	SSVQCTHG IKPVVSTQL	
		S A 7		F	N K	T	T R	
ri (UTATED AAS	5 M		r	T	•	÷*	
					•			

FIGURE 10

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coverneus - D		234
CONSENSUS-D	: btNNnSS	254
CONSENSUS-E	va	245
CONSENSUS-F		251
CONSENSUS-G		228
CONSENSUS-O		. 205
CONSENSUS-U	2 2D 2 2-2-2-H	120
CONSENSUS - CP	Z -????T??-?-?-???D-?-?-?-?-H?-?-?-?-?	120
	<- V3 neutralization loop	•
	^^^	
DECICNED SEC	LLNGSLAEE EIIIRSENLTNNAKTIIVHLNESVEINCTRP NNNTR K HYPERVARIABLE REGIO	N 3/4/5
DESIGNED SEQ	VV FDV Q K V S T	
MUTATED AAS	= -	
	LLnGSLAe???v?irSenitnNaktiiVql??pV?InCtRP.nnntr.ks???vri???gpGq??afya.	279
CONSENSUS - A	f Annbq_p	296
CONSENSUS-B	··	291
CONSENSUS-C	, _ 1	288
CONSENSUS - D		312
CONSENSUS - E	322 =Ah-Neg-G	302
CONSENSUS-F		305
CONSENSUS-G		39
CONSENSUS-H	IT-Skg.kIr-Mgk?dsg-NT-N-?i-mt-eg-?-v.Qei?mW-S.	279
CONSENSUS-O	IT-Skg.kIr-Mgk?dsg-NI-N-71-mL-E3	261
	IT-Skg.kIr-Mgk?dsg-NI-k	. 142
CONSENSUS-CP2	E.E-1MTN.	
V3 neu	tralization loop ->	

DESIGNED SEQ	HYPERVARIABLE REGION 3/4/5	
MUTATED AAs		
MOINILD 75.0		
CONCENCING - A	tgdiiG.dirgAhCnvsr?eWn?tlq?Va?qLr??f???nkt??iiF?n.ssGGD	320
CONSENSUS - A		342
CONSENSUS-B		. 334
CONSENSUS - C		331
. CONSENSUS-D		360
CONSENSUS-E		344
CONSENSUS - F		344
CONSENSUS-G		65
CONSENSUS-H		321
CONSENSUS-O	. +2nnKV*H*:*******************************	306
CONSENSUS-U		157
CONSENSUS-CPZ		
	CD4	
	HYPERVARIABLE REGION 3/4/5	
DESIGNED SEQ	HIPERVARIABLE REGION 3/1/	
MUTATED AAS		
	22 2222 22n2t2222 ???sndt I	355
CONSENSUS - A	lEitthsPnCggef?FYCnts?lF.nstW???????n?t.????????n?t???????sndtI	374
CONSENSUS - B		366
CONSENSUS-C		361
CONSENSUS - D		•
CONSENSUS - E		398
		372
CONSENSUS - F		373
CONSENSUS - G		92
CONSENSUS - H		356
CONSENSUS-0		336
CONSENSUS-U	?G??	175
CONSENSUS - CPZ	P-V??-?????-??????I	
	* CD4 (* . CD4	
DESIGNED SEQ	HYPERVARIABLE REGION 3/4/5	
MUTATED AAs		
בינת עוקרום		463
CONCENCIA 3	tlq.CrI.kqlvnm.wQrvgq.AmYapPIq.g?irc?sNITGllLTRDGg??nns??????	401
CONSENSUS - A		419
CONSENSUS - B		411
CONSENSUS-C	p::::::::	405
CONSENSUS - D	p	

FIGURE 10 (Cont)

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gp120 / gp41 TFRPGGGDIKDNWRSELYKYKVVKIEPLGVAPTR AKRRVV EREKRA VG IGAMIFGFLGA DESIGNED SEQ EK I K MUTATED AAS 462 CONSENSUS - A 480 CONSENSUS-B 470 CONSENSUS-C 465 CONSENSUS-D 508 CONSENSUS-E 478 CONSENSUS-F 481 CONSENSUS-G 187 CONSENSUS-H CONSENSUS-O CONSENSUS-U DESIGNED SEQ AGSTMGAASITLTVQAROLLSGIVQQQSNLLRAIEAQQHLLQLTVWGIKQLQARVLAVERYLKD QKFLG AGSTmGAaSiTLTvQarqL1SGIVqqQsN11rAIeaQqh1LkLTvWGIKQLQARvLAvErYLrD.QQLLG 531 CONSENSUS-A CONSENSUS-B 539 CONSENSUS-C CONSENSUS-D CONSENSUS-E 546 CONSENSUS-F 549 CONSENSUS-G CONSENSUS-H 529 CONSENSUS-0 CONSENSUS-U S NKSLEEIWNNMTWMEWEREISNYTNOIYE ILTESONOO DESIGNED SEQ LWGCSGKIICTTAVPWNSSW MUTATED AAS I IWGCSGK]ICtTnVPWNsSW....S.Nks??dIWdnMTWlqWdKEisnYT?iIY?.LiEesqnqQ 586 CONSENSUS-A 603 CONSENSUS-B CONSENSUS-C

CONSENSUS-D

CONSENSUS-E

CONSENSUS-F

CONSENSUS-F

CONSENSUS-G

CONSENSUS-G

CONSENSUS-O

CONSENSUS-O

CONSENSUS-O

CONSENSUS-U

CONSENSUS-U

CONSENSUS-U

CONSENSUS-U

CONSENSUS-U

CONSENSUS-U

CONSENSUS-CPZ

CONSENSU 589 636 603 606 580 555 DESIGNED SEQ DRNEQELLELDKWASLWNWFDITNWLWYIKIFIMIVGGLIGLRIVFAVLSIVNRVRQGYSPLSFQTLLPA MUTATED AAS KD A N SK V I I T 655 CONSENSUS - A 671 CONSENSUS - B 664 CONSENSUS-C 657 CONSENSUS - D 705 CONSENSUS-E 672 CONSENSUS - F 674 CONSENSUS-G 647 CONSENSUS-0 625 CONSENSUS-U CONSENSUS-CPZ -?-???-?E--?-?S-----T?----K--?-?-?1?----??????-??R?----?-?????-<- tat cds DESIGNED SEQ PRG PDRPEGIEEEGG EQDRDRSVRLVSGFLALAWDDLRSLCLFSYHRLRDLILI A AR IVELLGHS LGR

FIGURE 10 (Cont)

```
702
                                                               685
                                                               398
                                  <- rev cds
                    WEALKYL WNLLQYWGQELKISAVSLLNATAIAVAEGTDRVIEVAQRAGRAILHI
DESIGNED SEQ SLRGLRRG
                        WGLLNI
789
                                                               787
                                                               773
                                                               832
                                                               787
                                                               800
                                                               767
DESIGNED SEQ PRRIROGLERALL
MUTATED AAs
                                                              793
         PTRIRQGlEraLl$
CONSENSUS - A
                                                              801
         -?----F-a--g-
CONSENSUS - B
CONSENSUS - C
CONSENSUS - D
         -?---?----
                                                              845
CONSENSUS - E
                                                              79B
CONSENSUS - F
         ------
CONSENSUS - G
                                                              779
CONSENSUS - O
CONSENSUS-U ----F-----CONSENSUS-CPZ
```

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* CUIDD CE	MGGKWSKSSLVGWPEVRERIROT	PPAAEGVGAVSQD	LDKHGAITSSNTP	A
MUTATED AAS	C P A RA	A AR	Ā T Y	
ISOLATE-E	MGGKWSKSSIVGWPQVRERIKQT	PPAAEGVGAVSQD	LDKHGAVTSSNM	
CONSENSUS-A	MGGKWSKsSiVgWPeVrkRmRqT	.?PtaakgvgavsQD.	LDkhGAiTSSNt?	? 41
CONSENSUS-B	?-??era??????????????	?-EPOI APAAEGVGAASRD	LDKYGALTSSNTP	1 41 1
ISOLATE-C CONSENSUS-D	NT E-I-V-2222	dPDR	E'as	5 50
CONSENSUS-0	22.22 avan an 2 D2 22.2D	7-7PC-P??-RE.	A / K - G - / H - PC	, 36
CONSENSUS-U	NA??-?KF???-E-I-?-???	P?????	????-?-?-?? ?? A -	. 31
\vskip6pt	• SH3-binding SH3	-binding		
DESIGNED SEQ	NNADCVWLK AQE E EG VGFPVRPQVPLRPMTY P A E E	KGAFDLSFFLKEKGGI AV L	EGLVYSKKRQEILDLWV D I Q <u>D</u>	•
ISOLATE-E	NNADCVWLR AQE E EG VGFPVRPQVPLRPMTY	KGAFDLSFFLKEKGGI	EGLVYSKKRQEILDLWV	
CONSENSUS-A	tnpsCaWLE?Age?.de?.VGFPVRPOVPLRPMTY	-a-?	e:-qu	110 108
ISOLATE-C	THE PROPERTY OF THE VERDUDONDI POMTY	KAAFDLSLILKERGGU	FCT1 12 VVVCTE1 DDDWA	115
CONSENSUS-D	N-AAL-F-7.SH???	-e	2HA	93
CONSENSUS-U	N-AAL-F-?.SH??? N-??-?????E?E?		??	83
\vskip6pt	SH3-bind:	inq		٠.
	* 1 1	-		•
	YHTQGFFPDWHNYTPGPGIRY PLTFGWCFKLVPVDPI	REVE EINKGENNCLL	HPMSQHGMEDEEREVLI	
DESIGNED SEQ MUTATED AAS	$N ext{ } e$	S AL	ICD D K	
ISOLATE-E	YHTOGFFPDWHNYTPGPGIRY PLCFGWCFKLVPVDPI			
CONSENSUS-A	YnTOGE FPDWONYTPGPGERE . PLTFGWCEKLVPvDPa	EVE.eat?GEnNSLL	IPI COHGMODE? revim	176 174
CONSENSUS-B	-hy	kne	-msipe;	1/4
ISOLATE-C	YNTOGFFPDWONYTPGPGVRY PLTFGWCFKLVPVDPS	SEVE EINEGENMCDD	- ? E - pE - q k	182
CONSENSUS-D	-???S?E	-A-RIGNT?-?A?	-A-??E-?H?-I-?	150
CONSENSUS-O	-H???-?	,NC	-?S?-?Ei?	138
CONSENSUS-U	-н			
\vskip6pt	•	-		
PRATCHED SEO	WKFDSRLARRHIARELRPEFY KDC		•	
MUTATED AAS	H L M H Y			•
SOLATE-E	WKFDSALARRHIARELRPEFY KDC			
CONSENSUS-A	WkfDsrlalkhra?elhpefy.KDC\$			199
ONSENSUS-B	-rfh-m-ry?TSMCLQGTFRWG	I SREARLGGTGEWRAL	RCCI	230
SOLATE-C	WKFDSHLARRHMARELHPEYY KDC			206
CONSENSUS-D	-R-NfE-K-R-m			166
ONSENSUS-0	-?RS-G?T-???LF?-?			157
CONCENCITS -II	S??-?-R-??	_		

FIGURE 11

GAG OVERLAPPING SEGMENTS

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Segment 1	Segment 2	Segment 3	Segment 4	· Segment 5	Segment 6
MGARASVLSGGKLDAWEKIRLRPGGKKKY (K) atg ggc gcc agg ctc agg ctc agg gcc agg ttc ctc agm ggc ggc rag ctg gac gcc tgg gaa aag att agg ctc agg cct ggc gga aag aaa aag tat arg	WEKIRLBGGKKKYKMKHLVWASRELERFA RL - I	MKHLVWASRELERFALNPGLLETAEGOUGILETOEGOI L S K mtg aag cat mtc gtc tgg gct agc aga gag ctc gag aga ttc gct ctg aat ccc rgc ctg ctc gag aca kcc gaa ggc tgt mag caa att	LNPGLLETAEGCQQILEEQLQSALKTGSEEL SKGPPCccc ag gaa acc kct gag gga tgt maa cag atc ctg gra cag ycc gcc ctc mag aca ggc wcc gaa gag ctc	LEQLQSALKTGSEELKSLYNTIATLWCVHQ G P Q T R F V ctc grg caa ctg caa yct gct ctg maa acc gga wca gag gaa ctg arg tcc ctg twt aac aca itc gct acc ctc tgg tgt gtg cat cag	KSLYNTIATLWCVHQRIEVKDTKEALDKIE R F V ara ago ctc twc aat acc itc gcc aca ctg tgg tgc gtc cac caa agg att gas gtc arg gac aca aag gaa gcc ctc gac aaa atc gaa

F. I. E. V. K. D. I. K. E. A. L. D. K. I. E. E. E. Q. K. K. S. Q. Q. K. T. Q. Q. A. A. A. Segment 7 B. E. Q. K. K. S. Q. Q. K. T. Q. Q. A. A. A. D. T. G. S. S. K. V. S. Q. N. Y. P. I. V. Segment 8 V. N. N. K. S. Q. Q. K. T. Q. Q. A. A. A. D. T. G. S. S. K. V. S. Q. N. Y. P. I. V. S. Q. N. Y. P. I. V. Q. N. A. Q. G. Q. M. V. H. Q. P. L. S. P. R. Segment 9 D. T. G. S. S. K. V. S. Q. N. Y. P. I. V. Q. N. A. Q. G. Q. M. V. H. Q. P. L. S. P. R. Segment 9 Q. N. A. Q. G. Q. M. V. H. Q. P. L. S. P. R. T. L. N. A. W. V. K. V. I. E. E. K. G. F. N. Segment 10 L. Caa aac syc cag gga cag att gtg cat cag act mtt agc cct agg acc ctc aac gct tgg gtc aag gag aaa gag aac aga aac gas aaa gag acc act agg acc ctc aac gct tgg gtc aag gag aaa gag acc act acc gaa att ccc aga att gtg cat cag set mtt agc cct agg acc ctc aac gct tgg gtc aag gag aaa gag acc acc aga acc we cct aag acc ctc aac gct tgg gtc aag gag aaa gag att agc cct aag gac ctc aac gct tgg gtc aag gag aaa gag att agc cct aag gac ctc aac gct tgg gtc aag gag aaa gag acc acc aaa gcc tcg aac gcc aac gct tgg gtc aac gag gag aaa gcc tct acc gaa gag att ccc gaa gag acc ctc aac gct tgg gtc aac gag gac acc gaa agg gtc ccc aac acc gaa acc ccc aac acc ccc aac gcc tcg acc gcc gcc acc aac gcc tcg gcc gcc gcc acc aac gcc tcg acc gcc acc gaa gcc ccc aac gcc tcg gcc gcc acc gaa gcc gcc gcc acc gcc acc a

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	r tog atg aca art aac cot occ rto cot oto oga
Segment 17	STLQEQIGWMTNNPPIPVGDIYKRWIILGL A C V F
	a cag
Segment 16	ж э ы
	Γ . I I I I I I I I I I I I I I I I I I
Segment 15	EWDRVHPVHAGPIPPGQMREPRGSDIAGTT
	gag
Segment 14	AAMQMLKETINEEAAEWDRVHPVHAGPIPP
	Γ . Γ ect cag gat ctc aac ayg atg ctg aat ayt gtg gga ggc cat cag gcc gct atg caa atg ctg aaa gas aca atc aat gag gaa gcc gct
Segment 13	P Q D L N M M L N I V G G H Q A A M Q M L K E T I N E E A A
	Γ cct gag gtc atc cct atg ttc wca gcc ctc agc gaa ggc gct acc ccc caa gac ctg aat ayg atg ctc aac ayc gtc ggc gga cac caa
Segment 12	PEVIPMFSALSEGATPQDLNMMLNIVGGHQ

			21/	210	
Segment 18	Segment 19	Segment 20	Segment 21	Segment 22	Segment 23
PVGDIYKRWIILGLNKIVRMYQPVSILDI E ccc 9tg 99c gaw atc tat aag aga tgg atc att ctg 99a ctc aac aaa atc 9tg aga atg tat yma ccc gtc agc att ctg gat atc	KIVRMYQPVSILDIRQGPKEPFRDYVDRF S aag att gtc agg atg tac yma cet etc etc etc etc gac att arg caa ggc eet aag gaa eec ttt agg gat tac gtc gac aga ttc	QGPKEPFRDYVDRFYKTLRAEQATQEVKN For KN Cag gga cc asa gag ct tt aga gac tat gtg gat agg ttt twc asa acc ctc agg gct gag caa gcc wca cag gaw gtg asa aac	KTLRAEQATQEVKNWMTETLLVQNANPDC	MTETLLVQNANPDCKSILKALGTGATLEE D atg aca gaw acc etc etg gic cag aat gcc aat ecc gat tgc aag wee atc etc arg get etg gga mee gga gcc wea etg gaa gag	SILKALGTGATLEEMMTACQGVGGPSHKA T R D S G wca att ctg axa gcc ctc ggc mca ggc gct wcc ctc gag gaa atg atg aca gcc tgt cag gga gtg ggg ggc cct rgc cat aag gct
rt 🗢 H	N aat	저 저 R gra	ች ች ች	K 599	× × × × × × × × × × × × × × × × × × ×

Segment 24

TACQGVGGPSHKARVLAEAMSQATHANI G acc gct tgc caa ggc gtc ggc gga ccc rgt cac aaa gcc agg gtc ctg gca gag gct atg tcc cag gyg amc mac gct aac att

aga gtg ctc gcc gaa gcc atg agc caa gyc amc mat gcc aat atc atg atg cag aga ggc aat ttc ara ggc cma aag aga atc rtc aaa

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atg atg

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Segment 25

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Segment 26	Segment 27	Segment 28		Segment 29	
MMQRGNFKGQKRIIKCFNCGKEGHLARNCR RPV atg atg caa agg gga aac ttt arg gga cmg aaa agg att rtc aag tgc ttt aac tgt gga aag gaa ggc cat mtc gct arg aat tgc aga	R K K G C W K C G K E G 1	tgt ttc aat tgc ggc aaa gag gga cac mtt gcc ara aac tgt agg gcc cct aga aag agc tgt tgg aaa tgc gga arg gaa ggc cat APRKKGCWKCGKEGHQMKDCTERQANFLGK	ccc agg aaa aag gga tgc tgg aag	OMKDCTERQANFLGKIWPSNKGRPGNFPQS H	S caa atg aga gac tgt acc gaa agg caa gcc aat ttc ctc ggc aaa atc tgg ccc tcc mrc aaa ggc aga ccc gga aac ttt cyc caa agc

				23/2
Segment 30		Segment 31	Segment 32	Segment 33
GNFPQSKPEPTAPPAENFGFG L R	cct ggc aat ttc cyg cag tcc arg cct gag cct acc gct ccc cct gcc gaa arc ttt rga ttc ggc	AENFGFGETTTPSPKQEQKDKE QPt gag art ttc rgg ttc gga gag gaa acc aca cc tcc cma aag caa gag cma aag gat aag gag	QKDKEHYPPSASLKSLFGN.D P 1a cmg aaa gac aaa gaa cwc tac ccc cct tya gcc agc ctc aag tcc ctg ttt ggc aat gac	
д д К	se get eee ee	S P K Q	PPSASLKS L	
EE CF CF	cct gag cct ac	ETTP	YPPS L	KSLFGNDPLSQ
о 8 8 8	g cag tcc arg	FGFGE R ttc rgg ttc gga gag	KEHY) L	KSLFGNDPLSQ
Z F G J	c aat tto cy	ENFG SR t gag art ttc rg	Q K D P cmg and gac	L F G
አ ባ ርን	agg cct gg	PAE	K Q E	S L K S
X	S mrc aag gga	A P	PSP Q cct agc cmg	S A S L tya get tee
N S H	cct agc	E P	T T	ъ с с
I	att tgg	A R B ara cc	되 gaa gaa gaa	C. L. K

POL OVERLAPPING SEGMENTS

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Segment 1	Segment 2	Segment 3	Segment 4	Segment 5	Segment 6
FFRENLAFQQGKAREFSSEQTGANSSASRK TCttt agg gaa amc ctg gct ttc cmg caa ggc raa gcc aga gag ttt ycc agc gaa aga aca rga gcc aat agc gaa	SSEQTGANSSASRKLGDGGGAN	GDGGAEROGTSSFFPQITLWQRPLV:	SFPQITLWQRPLVTIKIGGQLKEALLDT(N V I I KTGCCCCC cag att acc ctc tgg cag aga ccc ctc gtg aca rtc aaa atc ggc gga cag ctc awa gag gct ctg ctc gac aca	I I I I I I I I I I I I I I I I I I I	r gac gat

FIGURE 12 (Cont)

Segment 12 Segment 9 gg cag mtt ggc ygc acc ctc aac ttt ccc att agc atg gat ggc ggc aga Ö Z, S S 召 gga aag att atc aaa × Д \mathcal{O} Н A, att ¥ Σ Д × \mathbf{H} gga aaa aat atc U \mathcal{O} 노 Ŀ × Н 9ag gag S gga Ы Д 闰 Z Z Ö Vaa cct gtg aaa ctg aaa acc gaa acc cct gtg 田区区 ᄓ × 回 > C gag 回 E Д ⊣ ctc × П Σ CV 団 [-686 Ü cct 闰 μ Ö Ω_{i} ama t.99 att gtg gga X H ΗД Д 3 Ö cag tgc aca gtg Ö O O > > aaa gtg ctc \vdash × Н O Ц 959 口 回 sep 9119 ate gga agg aae mtg etg gac 田及 > П > aaa aca att ggc aca tat X \vdash Σ \Box CCC gaa aag att aag get etg S cag Н Z Д Д Ü Ø gga atc tcc att Ø r α ß Н œ gac gtc × Ö $\boldsymbol{\vdash}$ Ω K > gar atg aaa Д Σ Н ĸ 990 maß ccc gtc aac att tto atc ĸ K(H) Ö Н Ŀ aat g 266 口 Д Z Z O [z, aag ctg aca gag tgc 990 团 ¥ Ы U > Ö ata aca att \vdash Н Ы Д O Н aag ctg ygc ccc aca C K ¥ П \vdash 口 CCt gtc 99a 990 att Д Ö Д Н Ö tgg ig ig gtc ctg gtc ggc S ᆲᆔ gga 3 Д G Ö caa Caa O > Ø > \vdash Н cag × ₽ П O Σ gtc oto 口田縣 > > Ы Ω 幺 atg acc tac × Η \succ Д SC 99a aat Д щ Z r ¥ O

Segment 13	Segment 14	Segment 15	Segment 16		Segment 17	
LTEICKEMEEEGKISKIGPENPYNTPVFAI AT K Q Ctc acc gmg atc tgt ama gaa atg gaa vaa gaa ggc aaa atc tcc arg att ggc cct gag aat ccc tat aac aca ccc rtc ttt gcc att	KIGPENPYNTPVFAIKKDSTKWRKLVDFRR R . arg atc gga ccc gaa aac cct tac aat acc cct rtc ttc gct atc aag gac tcc acc aaa tgg aga aag ctc gtg gat ttc aga	K K K D S T K W R K L V D F R E L N K R T Q D F W E V Q L G	aaa aag aaa gat agc aca aag tgg agg aaa ctg gtc gac ttt agg gag ctc aac aaa agg aca cag gtt ttc tgg gag gtc cag ctc ggc	gaa ctg aat aag aga acc caa gac ttt tgg gaa gtg caa ctg gga atc cct cac cct gct gga ctg aaa aag aaa aag tcc gtg aca gtg	I P H P A G L K K K K S V T V L D V G D A Y F S V P L D E S K D	G att ccc cat ccc gcc ggc ctc aag aaa aag aaa agc gtc acc gtc ctg gat gtg gga gac gct tac ttt agc gtc ccc ctc gac xaa rxc

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27/216 Segment 19 Segment 20 Segment 22 IFQSSMTKIL
PQ gag cct cag gga tgg atg gtc atc tat cag tat ≊ 耳 gaa atc gga cag Ö Ø O O Q $H \vdash$ Д cct agc tat aac gtc ctg Ы 回 gtg att tac caa tac atg gac gat ctg tat gtg gga agc gat ctg Σ 口 aca atc E D Z \Box ttt agg awa maa aac cct Д ഗ O Z r gat ggc att agg tat × X Q > tat acc 228 222 α A A Н Д R 口 aga aag ta Ö Ŋ ہتا Ω gct cct аад дда Д \mathcal{O} D, Ω acc H × 回 Σ cct ctg gat raa rrc gaa ctc ccc caa ggc tgg SDB 闰 3 H aac att Z \mathcal{O} Ø S I N D T tcc ayc aat a X Ore ga O ⊱ 는 어 ga Д Ы Σ > gtg tat ttc tcc gtg ပ္ပ atg > Ŋ Σ gcc ttt acc att tac aat 田口幣 Н Z Ŋ S Н ≻₁ Ø Д tac caa tt [L Q ſι Z 900 X Or g Ø × gat atc aga **⊄**(0,000 to 0,000 t tac aca H X ẫ [-- α 366 aga \vdash Д α gtc gga × Ö ഗ ſι ပ္ပပ္ပ Ü α Д Ö Д

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Segment 23

Ö Z വ ᆸ ᆟ 工 ø 民 П 闰 回 Н × ⊣ ĸ 二 Ø Ŋ Н 臼 Д Д ഗ r \gt \succ П Ω Ω Σ

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	Segment 24		Segment 25		Segment 26	•	Segment 27	
m A $ m E$ $ m K$ $ m Q$ gac etc gag att ggc caa cac agg rcc aaa atc gaa gag etc agg sma cac etc etg ara tgg gga	IEELRAHLLRWGFTTPDKKHQKEPPFL E K	aag att gag gaa ctg aga smg cat ctg ctc ara tgg ggc ttc aca acc cct gac aaa aag cat cag aaa gag cct ccc ttt ctg	PDKKHQKEPPFLWMGYELHPDRWTVQP	aca ccc gat aag aaa cac caa aag gaa ccc cct ttc ctc tgg atg gga tac gaa ctg cat ccc gat agg tgg acc gtc cag cct	YELHPDRWTVQPIELPEKDSWTVNDIQ V	ggo tat gag oto cao oot gac aga tgg aca gtg caa ooc ato swg oto ooc gaa aag gas too tgg aca gtg aat gao att cag	PEKDSWTVNDIQKLVGKLNWASQIYAG E	cct gag aaa gaw agc tgg acc gtc aac gat atc caa aag ctc gtg gga aag ctc aac tgg gcc tcc cag att tac
atg gat g	HA X	aga rca a	F T T	ttt acc a	M M	tgg atg g	H V V	Q att swg ctg
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Segment 28	Segment 29	Segment 30	Segment 31	Segment 32	Segment 33
KLVGKLNWASQIYAGIKVKQLCKLLRGTKA P aaa ctg gtc 99c aaa ctg aat t99 gct agc caa atc tat 8ct 99c atc aaa 9tg arg caa ctg tgt aag ctc ctg aga 99c rcc aaa 9cc	IKVKOLCKLLRGTKALTDIVPLTEEAELELL A att aag gtc ara cag ctc tgc aaa ctg ctc agg gga rca aag gct ctg aca gas att gtg mca ctg aca gag gaa gcc gaa ctg gaa ctg	LTDIVPLTEEAELELEERREILREPVHGVY E T ctc acc gaw atc gtc mca ctc acc gaa gag gct gag ctc gag ctc gmg gaa aac aga gag att ctg axg gaa ccc gtc cac gga gtg tat	EENREILREPVHGVYYDPSKDLVAEVQKQG A 9mg gag aat agg gaa atc ctc ara gag cct gtg cat ggc gtc tac tac gat ccc tcc aag gat ctg rtc gct gaa rtc caa aag caa ggc	YDPSKDLVAE $\overrightarrow{(V)}$ QKQGQDQWTYQIYQEPFKNIG Gabor cot ago as a gao ct to ago as a cag ago cot to a a a act	QDQWTYQIYQEPFKNLKTGKYSRKRSAHTN G F F F caa grc caa tgg acc twc caa atc twt cag gaa ccc ttt aag aat ctg aaa acc gga aag tat kcc aga awg aga rgc gct cac aca aac

Segment 34	Segment 35	Segment 36	Segment 37	Segment 38	Segment 39
L K T G K Y S R K R S A H T N D V R Q L T E V V Q K $\stackrel{\cdot}{I}$ A T E A $\stackrel{\cdot}{V}$ A $\stackrel{\cdot}{V}$ A A ctc ang acc ggc as a tac kct agg awg agg rgt gcc cat acc aat gac ctc arg caa ctg aca gmg gyt gtg caa aag rtt gcc aca gag	DVRQLTEVVQKIATESIVÄIWGKTPKFRLPI K K gat otg ara cag otc acc gma gyc gtc cag aaa rtc gct acc gaa agc att gtg att tgg gga aag aca ccc aaa ttc ara ctg cct atc	SIVIWGKTPKFRLPIQRETWETWWMEYWQA K K A TD tcc atc gtc atc tgg ggc aaa acc cct aag ttt arg ctc ccc att cag ara gag aca tgg gaa rcc tgg tgg ayg gas tat tgg caa gcc	QRETWETWWMEYWQATWIPEWEFVNTPPLV K caa arg gaa acc tgg gag rct tgg tgg tgg tgg cag gct acc tgg atc cct gag tgg gag ttt gtg aat acc cct ccc ctc gtg	TWIPEWEFVNTPPLVKLWYQLEKDPIVGABE ANDFIVGAE as a sas etc egg etc egg etc eng	KLWYQLEKDPIVGAETFYVDGAASCRETKLG EAV Naaa ctg tgg tac caa ctg gaa aag gam ccc att gyc gga gyc gaa acc ttt tac gtc gac gga gcc gct arc aga gag aca aag ctc ggc

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Segment 46	Segment 47	Segment 48	Segment 49	Segment 50
EKVYLSWVPAHKGIGGNEQVDKLVISGIRK R gag ara gtg tat ctg kct tgg gtc ccc gct cat aaa ggc att ggc gga aac gaa cag gtc gac aaa ctg gtc akc kct ggc att agg aaa	GNEQVDKLVISGIRKVLFLDGINKAQEEHE SA ggc aat gag caa gtg gat aag ctc gtg akt kcc gga atc aga aag gtg ctc ttc ctc gac gga atc rat aag gct cag gaa gag cac gaa	V L F L D G I N K A Q E E H E R Y H S N W R T M A S D F N L K A Q C caa gag gaa cat gag arg tat cac toc aac tgg agg aca atg got arc gam tto aat ctg	RYHSNWRTMASDFNLPPIVAKEIVANCDKC K ara tac cat agc aat tgg aga acc atg gcc art gas ttt aac ctc ccc cct atc gtc sct aag gaa atc gtc gcc wrt tgc gat aag tgt	PPIVAKEIVANCDKCQLKGERAMHGQVDCSPPPIVB I N CCC att gtg scc aaa gag att gtg gct wrc tgt gac aaa tgc cag ctc aag gga gag gct atk cac gga cag gtc rac tgt agc cct

			33/	216	
Segment 51	Segment 52	Segment 53	Segment 54	Segment 55	Segment 56
Q L K G E A M H G Q V D C S P G I W Q L D C T H L E G K V I I N I caa ctg aaa ggc gaa gcc ats cat ggc caa gtg rat tgc tcc ccc ggc att tgg caa ctg gat tgc aca cac ctc gag gga aag rtt atc	GIWQLDCTHLEGKVILVAVHVASGYIE BAEV I gga atc tgg cag ctc gac tgt acc cat ctg gaa ggc aaa rtc att ctg gtc gcc gcc gcc tcc ggc tac att gag gct gag gtc	LVAVHVASGYIE AEVIPAETG QETAYFLLK I.	IPAETGQETAYFLLKKAGRWPVKVIHTDNG I att ccc gct gag aca ggc caa gag aca gcc tat ttc mtt ctg aaa ctg gct ggc aga tgg cct gtg ara ryc att cac aca gac aat ggc	LAGRWPVKVIHTDNGSNFTSAAVKAACWWA RT ctc gcc gga agg tgg ccc gtc arg rya atc cat acc gat aac gga agc aat ttc aca agc rct rcc gtc aag gct gcc .tgc tgg tgg gct	SNFTSAAVKAACWWANIKQEFGIPYNPQSQQQQQqqqqqqqqqqqqqqqqqqqqqqqqqqqqqqq

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Segment 66 Segment 64 Segment 65 Segment 63 GEGAVVIQDNSDIKVPRRKAKII \Box gaa ggc gct gtg gtc atc caa Ø A, Ö 凶 r aaa × gac gaa gac О 臼 口 Ω gmt gac tgt gtg gct rgc agg caa O × α Ø cct ប្រ ល ρ, Þ Ö > U ⋈ Ω D A $\rho_{\mathbf{i}}$ gat tac gga aag caa atg gct ggc $\boldsymbol{\wp}$ Д ø α Σ വ ⊼ aag Ø Д L W I \bowtie \mathcal{O} A K L] \Box α

VIF OVERLAPPING SEGMENTS

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Segment 1	Segment 2	Segment 3	Segment 4	Segment 5
	ρ O gas	υ υ	SEVHIPLGEARLVIRTYWGLQTG DIK H	TYWGLOTGEKDWOLGHGVSIEWR Sactat 199 99a ctg caw acc gga gag ara gac tgg cas ctc 99c caw 99c gtc agc att gag tgg agg
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I R T W N S L V K H H M Y K Att agg aca tgg aaw agc ctc gtg aaa cac cat atg yat	HHMYISKKAKGWFYRHHY H g cat cac atg yac atc tcc aag aaa gcc aaw ggc tgg ttc tat agg cat cac tw	FYRHHYESQHPKVSSEVHIPLG	EVHIPLGEARLVIRTYWGLQT DIK H	TYWGLOTGEKDWOLGHGVSIEW H R H Q acc tat tgg gga ctg caw acc gga gag ara gac tgg cas ctc ggc caw ggc gtc agc att gag tg
W tgg	A K (N gcc aaw	V y gto	H G	s ct
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C gt		}; ₽	> sa	at to
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37/216

Segment 10 V R R R C E Y P S G H N K V G S L Q Y L A L Q Y L A L Q to aga sg a agg tgt gag tat cmg kcc gga cac aat aag gtc ggc tcc ctg caa tac ctc gcc ctc cct aag aaa atc ara ccc cct ctg cct agc ഗ gga cas aka gtg agm agg aga tgc gaa Д 闰 Ц U Д R Д 召 요 도 വ വ > Н нα × OH Д Ö aac aaa gtg gga agc ctc cag tat ctg gct ctg amg gct ctg att amg aga gcc att ctg П Н Ы Z, Ø α X F α Ы ø HK Ы ß gac Д χĊt Ø SA П ш S U H R caw aka Ö Ω > Ŀ gct atc ctc ggc Ö × OH > ᆸ Z 出 Ц G 工 Ø, agg kg A S 民 Н

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Segment 11		Segment 12	
EDRWNKPQKI	${ m K}$ ${ m E}$ ${ m T}$ aag att arg cct ccc ccc tcc gtg aaa aag ctc acc gaa gac ara tgg aat rag cct caa aag aya	н в	arg tgg aac raa ccc cag aaa ayc aag gga crc aga gra aat cac aca atg aat ggc cat
R W	K c ara tgg	NHIMNG	c aca atg
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저	rg cct	N N N	ac raa
M H	Att a	M M	tgg a
X X	aa aag	U K K	jat arg
P R	GCC &	四	gag
E H	K tc ama	[⊣	tg ace
	K gcc ctc atc ama ccc aaa	X	aaa c
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VPR OVERLAPPING SEGMENTS

		39/216	i
Segment 1	Segment 2	Segment 3	Segment 4
APEDQGPQREPYNEWALELLEELKQEA Segr SS	gct ccc gaa gac caa rgc yct cag aga gag cct tac aat gag tgg rcc ctc gag ctc ctg gaa gag ctc aag mam gag gct A L E L L E E L K Q E A V R H F P R P W L H \widehat{N} L G Q \widehat{Y} T H G X R H F P R P R P W L H \widehat{N} L G Q \widehat{Y} T N S R H F P R P R P W L H \widehat{N} L G Q \widehat{Y} T R R H F P R P R P W L H \widehat{N} L G Q \widehat{Y} T R R H F P R P R P W L H \widehat{N} L G Q \widehat{Y} T R R H F P R P R P W L H \widehat{N} L G Q \widehat{Y} T R R H F P R P R P W L H \widehat{N} L G Q \widehat{Y} T R R H F P R P R P W L H \widehat{N} L G Q \widehat{Y} T R R H R P P R P R P W L H \widehat{N} L G Q \widehat{Y} T R R R P R P R P W L H \widehat{N} L G Q \widehat{Y} T R R R P R P R P R P R P R P R P R P R	FPRPWLHNLGQYIYETYGDTWSGVEALL GPRPROGRAGE CCC A GOVEAL CCCC A GOVEAL CCCC A GOVEAL CCCC A GOVEAL CCCCC A GOVEAL CCCCC A GOVEAC CCCC A GOVEAC CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	TYGDTWSGVEALIRTLQQLMFIHFRIG Segr
ы О	(g gaa cag	A agg	∃ >>
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FIGURE 12 (Cont)

att tac gaa acc tat ggc gat acc tgg kma ggc gtc gag gct ctg atc aga ayc ctc cag caa ctg mtg ttt rtc cat ttc aga atc gga

FIGURE 12 (Cont)

Segment 5		Segment 6
HFRIGCQHSRIGILRQRRAR S I G	mtg ttc xtt cac ttt agg att ggc tgc crg cac tcc agg att ggc att myc aga cag aga agg gsc aga	8
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TAT OVERLAPPING SEGMENTS

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Segment 6

Cont)

RE 12 (Cont)

QTRGGNPTDPKESKKEVASKTETDPCDPCDPDCDPCDPCDPCDPCDPcaa mcc aga ggc grt aac cct acc grt ccc raa gag tcc aag gtc gmg tcc aag rca gag aca gac cct tkt gac

* different

REV OVERLAPPING SEGMENTS

		43/	216	
Segment 1	Segment 2	Segment 3	Segment 4	Segment 5
GRSGSTDEELLRAVRIINILYQSNPYPS D N 990c Aga agc gga rrc aca gac gaa gag ctc ctg arg gct rtc aga atc att aas att ctg tat cag tcc aac cct tac cct wcc	IINILYQSNPYPSSEGTRQTRKNRRRW K att atc aaw atc ctc tac caa agc aat ccc tat ccc wca agc gaa ggc wcc agg caa rcc aga arg aat agg aga agg aga tgg	GTRQTRKNRRRRWRARQRQIRAISERIL SAR H 99a wca aga cag act agg ara aac aga agg aga agg tgg agg gmg agg caa agg caa atc crc kcc atc tcc gag wgg att ctg	ROROIRAISERILSTCLGRSAEPVPLOL HS W NF P	CLGRSAEPVPLQLPPLERLHLDCSEDCG F Kk ctg gga agg yct gcc gaa ccc gtc ccc ctc cag ctc ccc cct ctg gaa agg ctc mac ctc gac tgt agc gaa gac wgt grc
	5 1	E G	A R E gma ag	ans R H
M A	V R I rtt ag	ស ពួ	R 7 B aga g	S T

Segment 6			Segment 7				Segment 8	
ტ		ctg gat tgc tcc gag gat wgc grt acc tcc ggc aca cag caa agc caa ggc aca gag aca gga gtg gga	Ŋ			ctc ggc ycc gga		
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⊢		a ace	П			Ctc		
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VPU OVERLAPPING SEGMENTS

Segment 1	Segment 2	Segment 3	Segment 4	Segment 5
MTPLEIIAIVAFIVALIIAIVWTIAYIEY at BY Set atc mta gcc att gtg gtc tgg aca atc gyc two att gag tat	LIIAIVVWTIAYIEYRKLLRQRRIDRLIKR L ctg att mtc gct atc gtc gtg tgg acc att gyg twt atc gaa tac arg aaa ctg ctc arg caa agg ara atc gat agg utc atc raa agg	RKLLRQRRIDRLIKRTRERAEDSGNESEGD (K) K K E I E I ara aag ctc ctg ara cag aga arg att gac aga ctg att rag aga ayc aga gac gac gac tcc ggc aat gag tcc gag gga gac	TRERRAEDSGNESEGDTEELSTMVDMGNYDL I aya agg gaa agg gct gag gat agc gga aac gaa agc gat asa gaa gag ctc agc rca wtg gtc gac atg ggc aat tac gat ctg	TEELSTMVDMGNYDLGVDNNL R asa gag gaa ctg tcc rcc wtg gtg gat atg gga aac tat gac ctc ggc gtc gac aat aac ctc

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ENV OVERLAPPING SEGMENTS

E T O N a gag aca cag a I L G I y atc ctc ggc v V T V T L F G aca ctg ttt H N V tg cat aac gtc T P Q E	E T Q N gag aca cag a I L G I atc ctc ggc v V T V V Gt acc gtc f Cat acc gtc c Cat acc gtc c	2 6 112 7	N W P N L W K W G T L I L G L V I T C S A S A S A S A S A S A S A S A S A S	H P N L W K W G T L I L G L V I T C S A S A S A S A S A S A S A S A S A S	P N L W K W G T L I L G L V I I C S A S A S C and the grant ctg gga mtg gtc ats att tgc tcc gcc tcc at ctg tgg arg tg aca mtg att ctg gga mtg gtc ats att tgc tcc gcc tcc by a S B A S D N L W V T V Y Y G V P V W R B B A D T T L F C A S D A K A H E T T C C A S D A K A H A C C G C Gtc tgg agg gcc cc gcc tgg ggg aca acc ctc ttc tgg gcc aca ccc gcc tgg gcc aca acc ctc ttc tgg gcc aca ccc gcc tgg gcc aca acc ctc ttc tgg gcc aca ccc gcc tgc gcc aca ccc gcc tgg gcc aca ccc gcc tgc gcc aca	A L W K W G T L I L G L V I I C S A S A S A S A A A A A B A B A B A B A	Li W K W G T L I L G L V I I C S A S C c c grad and grad c c c c c c c c c c c c c c c c c c c	R R R R R R R R R R R R R R R R R R R	Fig. 69 GyC aca mtg att ctg gya mtg gtc ats att tyc tcc gcc tcc gyc gyc ats att tyc tcc gcc tcc gyc gyc ats att tyc tcc gyc tcc gyc tcc gyc tcc gyc tcc gyc gyc gyc ats att tyc tyc gyc tcc gyc tcc gyc tcc gyc gyc gyc aca gyc tat tac gya gyc cct gyc gyc gyc aca gyc tat tac gya gyc cct gyc	G T L I L G L V I L C S A S S M M M M M M M M M M M M M M M M	T L I L G L V I T C S A S N M M gc aca mtg att ctg gga mtg gtc ats att tgc tcc gcc tcc L W V T V Y Y G V P V W R at ctg tgg gtg aca gtg tat tac gga gtg cct gtg tgg agg D T T L F C A S D A K A H T Ct rmc aca acc ctc ttc tgt gcc tcc gac gct aag gct yac ca gag gtc cac aat gtg tgg gcc aca cac gct tgc gtc ccc y V gt ccc aat ccc caa gag rtt swc ctc gag aat gtg aca gag N W W M W K N M W E Q M Q E Ct rac aat gtg tgg gcc aca cac gct tgc gcc ccc D A H Ct rac aat ccc caa gag rtt swc ctc gag aat gtg aca gag R M W K N M W W C C M C M C M Ct rac aat ccc caa gag rtt swc ctc gag aat gtg aca gag Ct rac aat ccc caa gag rtt swc ctc gag aat gtg aca gag Ct rac aat ccc caa gag rtt swc ctc gag aat gtg aca gag Ct rac aat ccc caa gag rtt swc ctc gag aat gtg aca gag Ct rac aat ccc caa gag rtt swc ctc gag aat gtg aca gag	L I L G L V I T C S A S M M M M M M W R W V T V Y Y G V P V W R T T L F C A S D A K A H V H N V M A T H A C V P N P Q E I H L E N V T E V M W W M T M W B T H A C G G G G G G G G G G G G G G G G G G	I L G L V I I C S A S M M M M g att ctg gga mtg gtc ats att tgc tcc gcc tcc V T V Y Y G V P V W R g gtg aca gtg tat tac gga gtg cct gtg tgg agg T L F C A S D A K A H Y A C C C tc tc tgt gcc tcc gac gct aag gct yac H N V M A T H A C V P T C C C C C C C C C C C C C C C C C C N V V A C C C C C C C C C C C C C C C C C C	C C C C C C C C C C	G L V I I C S A S M M gga mtg gtc ats att tgc tcc gcc tcc V Y Y G V P V M R gtg tat tac gga gtg cct gtg tgg agg F C A S D A K A H Y ttc tgt gcc tcc gac gct aag gct yac V M A T H A C V P gtg tgg gcc aca cac gct tgc gtc ccc E I H L E N V T E V V a gag rtt swc ctc gag aat gtg aca gag N M W E Q M Q E D H A aac rat atg gtc gac caa atg caa gag	N I C S A S	N	A ats att tgc tcc gcc tcc G V P V W R gga gtg cct gtg tgg agg C D A K A H Y C gac gct aag gct yac T H A C V P aca cac gct tgc gtc ccc L E N V T E C gag aat gtg aca gag V C G G G G G G G G G G G G G G G G G G	att tgc tcc gcc tcc / P V W R gtg cct gtg tgg agg gac gct aag gct yac H A C V P cac gct tgc gtc ccc gag aat gtg aca gag gag aat gtg aca gag E O M O E D H	Ege tee gee tee V W R Cet gtg tgg agg Cet gtg tgg agg Get tgc gtc ccc	A S cc gcc tcc W R ttg tgg agg ttg tgg agg gtg aca gag f Q E H H Agg aca gag atg caw gag	Cc tcc Cc tcc Cc tcc Cc tcc Cc C	
R V K aga gtg aa G T L M gga acc w aac etc t acc crmt a T E \ T E \ D P \ D P P	K M W W W W M M M M M M M M M M M M M M	I I I I I I I I I I I I I I I I I I I	2 8 1123 11 2 2	N aaac V V Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y	K A A A A A A A A A A A A A A A A A A A	D O D D Bat H H H H	A A B B B B B B B B B B B B B B B B B B	C C C C C C C C C C C C C C C C C C C	R K K K K K K K K K K K K K K K K K K K	M P P P P P P P P P P P P P P P P P P P	D 2 2 2 2 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3	T at ct I I I I I I I I I I I I I I I I I I	M W W W W A B B B B B B B B B B B B B B B	H H H H C C C C C C C C C C C C C C C C	L L L C ctc C ctc C ctc R K K K K K K K K K K K K K K K K K K	G G G G G G G G G G G G G G G G G G G	M M W W M M M C C C C C C C C C C C C C	Y N A GCC GCC GCC GCC GCC GCC GCC GCC GCC G	A ats S I T I T I T I T I T I I T I I I I I I	H H H H H D D D D D D D D D D D D D D D	S : ggc t : gg	M W W W W M M M M M M M M M M M M M M M	Cc tcc RR H K K K K K K K K K K K K K K K K K
E T Q M N W P N L W K W G T M R R R R R R R R R	E T Q N gag aca cag a I L G I atc ctc ggc v V T V V Gt acc gtc f Cat acc gtc c Cat acc gtc c	2 6 112 7	N W P N L W K W G T L I L G L V I I C S A S asc teg ccc aat ctg teg arg teg ggc aca mtg att ctg gga mtg gtc ats att tgc tcc gcc tcc V I I C S A S D N L W V T V Y Y G V P V W R M R A S D N L M V T L F C A S D A K A H E T E T C A S D A K A H E T E V H N V W A T H A C V P Y D gct agc gat gcc asa gcc yst gas aca gg gtc cac act gtg teg gcc aca cac gct tgc gtc ccc A T H A C V P T D P N P Q E I H D C S C S S S S S S S S S S S S S S S S	H P N L W K W G T L I L G L V I T C S A S A S A S A S A S A S A S A S A S	P N L W K W G T L I L G L V I I C S A S A S C C aat ctg tgg arg arg etc gga mtg gtc ats att tgc tcc gcc tcc at ctg tgg arg arg tgg gtg aca gtg tat tac gga gtg cc c gcc tgg tgg gtg aca gtg tat tac gga gtg cct gtg tgg gtg aca gtg tat tac gga gtg cct gtg tgg agg gtg aca gtg tat tac gga gtg cct gtg tgg agg gtg aca gtg tat tac gga gtg cct gtg tgg agg gtg aca gtg tat tac gga gtg cct gtg tgg agg gtg aca gtg tat tac gga gtg cct gtg tgg agg agg aca gtg tat tac gga gtg tat tac gga gtg tgg agg agg aca acc ctc ttc tgt gcc tcc gtg tgg agg agg gtc cc aa acc ctc ttc tgt gcc tcc gac gct aag gct yac C C A B B A B A B A B A B A B A B A B A	N L W K W G T L L G L V I T C S A S	Li W K W G T L I L G L V I I C S A S Rectg tgg arg tgg aca mtg att ctg gga mtg gtc ats att tgc tcc gcc tcc S A S D N L W V T V Y Y G V P V W R E	R	Fig. 69 GyC area mtg att ctg gyaa mtg gtc ats att tyc tcc gcc tcc gyc gyc ats att tyc tcc gcc tcc gyc gyc ats att tyc tcc gyc tcc gyc tcc gyc tcc gyc gyc gyc gyc ata at tac gya gyc gyc gyc at gyc	G T L I L G L V I L C S A S M M M M gg ggc aca mtg att ctg gga mtg gtc ats att tgc tcc gcc tcc N L W V T V Y G V P V W R as aat ctg tgg gtg aca gtg tat tac gga gtg cct gtg tgg agg T T L F C A S D A K A H N L W N M A T H A C V P In B y H N V W A T H A C V P In B y H N V W A T H A C V P In B y C T T T T T T T T T T T T T T T T T T	T L I L G L V I T C S A S N M M Re aca mtg att ctg gga mtg gtc ats att tgc tcc gcc tcc L W V T V Y Y G V P V W R at ctg tgg gtg aca gtg tat tac gga gtg cct gtg tgg agg D T T L F C A S D A K A H T Ct rmc aca acc ctc ttc tgt gcc tcc gac gct aag gct yac ca gag gtc cac aat gtg tgg gcc aca cac gct tgc gtc ccc y V gt ccc aat ccc caa gag rtt swc ctc gag aat gtg aca gag N W N M W K N M W E Q M C F D D H H Ett aac atg tgg aaa aac rat atg gtc gas caa atg caa gag H H H H H H H H H H H H H	L I L G L V I T C S A S M M M M M M W R W V T V Y Y G V P V W R T T L F C A S D A K A H V H N W M A T H A C V P N P Q E I H L E N V T E V W M M M T B D B C M W K N M W W E Q R C aat CCC caa gag rtt swc Ctc gag aat gtg aca gag C aat CCC caa gag rtt swc Ctc gag aat gtg aca gag M W K N M W E Q M Q E D D H Ac atg tgg aaa aac rat atg gtc gtc caa atg caa atg caa gag R W K N M W W E Q M Q E D H	I L G L V I I C S A S M M M M g att ctg gga mtg gtc ate att tgc tcc gcc tcc V T V Y Y G V P V W R g gtg aca gtg tat tac gga gtg cct gtg tgg agg T L R C A S D A K A H Y a acc ctc ttc tgt gcc tcc gac gct aag gct yac H N V M A T H A C V P t c cac aat gtg tgg gcc aca cac gct tgc gtc ccc V V N V At ccc caa gag rtt swc ctc gag aat gtg aca gag W K N M M V E Q M Q E D H g tgg aaa aac aat atg gtg aca atg gcg aca gag		G L V I I C S A S M M gga mtg gtc ats att tgc tcc gcc tcc V Y Y G V P V M R gtg tat tac gga gtg cct gtg tgg agg F C A S D A K A H Y ttc tgt gcc tcc gac gct aag gct yac gtg tgg gcc aca cac gct tgc gtc ccc E I H L E N V T E V V a gag rtt swc ctc gag aat gtg aca gag N M W E Q M C F O D H A aac rat atg gcc ga aat gtg aca gag	N I C S A S	N	A ats att tgc tcc gcc tcc G V P V W R gga gtg cct gtg tgg agg C D A K A H Y C gac gct aag gct yac T H A C V P aca cac gct tgc gtc ccc L E N V T E Ctc gag aat gtg aca gag V C G M Q E D H Gtc gas caa atg caw gag	att tgc tcc gcc tcc / P V W R gtg cct gtg tgg agg gac gct aag gct yac cac gct tgc gtc ccc cac gct tgc gtc ccc cac gct tgc gtc ccc E N V T E gag aat gtg aca gag E Q M Q E D H	Ege tee gee tee V W R Cet gtg tgg agg Cet gtg tgg agg Get tge gte eec Get tge gte eec Get tge gte eec M V T E A V T T E A V T T E A V T T E A V T T E A V T T E A V T T E A V T T E A V T T E A V T T E A V T T T E A V T T T T T T T T T T T T T T T T T T	A S cc gcc tcc W R ttg tgg agg ttg tgg agg cc yac tgc gtc ccc	Cc tcc R H Y yet yac T T T T T T T T T T T T T T T T T T T	

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FIGURE 12 (Cont)

Segment 7			Segment 8		Segment 9
V E Q M Q E D V I S L W D Q S L K P C V K	H	atg gtg gam cag atg cam gaa gac rtt atc tcc ctg tgg gac caa agc ctc aag cct tgc gtc aag	LKPCVKLTPLCVTLNCTNANL	tcc ctg aaa ccc tgt gtg aaa ctg aca ccc ctc tgc gtc acc ctc aac tgt acc aat gcc aat ctg	N C T N A N L I N V N
ы С	H	cam gaa	V K	gtg aaa	N L
M O	_	lam cag atg	C D	laa ccc tgt	l N A
M V E	Ц		SL	tee etg a	
z	Д	aat rac	Q	tgg gat cag	L
X N		aag	M	tgg g	V
Z		ttc aat atg tgg	ᆸ	agc ctc	C. C.
N		aat at	H S		P C C C C
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GAP IN SEGMENTS DUE TO HYPERVARIABLE REGIONS 1 AND 2

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Segment 1	Segment 2		Segment 3	Segment 4		Segment 5	
YRLINCNTSVIKQACPKVSFDPIPIHYCTPPP SAT tac aga ctg att arc tgt aac aca age gyt atc ama cag gct tgc cct aag rtt asc ttt gas cct atc cat tac tgt rcc cct	PKVSFDPIPIHYCTPAGYAILKCNDKNFNG IT E A F F T N K	: cac tat tgc xct ccc gcc gga twc gc KNFNGTGPC	m N $ m K$ $ m T$ $ m T$ $ m T$ $ m Secondary Constraints and sat grant acc gga acc gga acc tgt amg aat gtg tcc asc$	TGPCKNVSSVQCTHGIKPVVSTQLLLNGSL T T T R	aca ggc cct tgc ama aac gtc agc wcc gtg caa tgc aca cac gga atc ara ccc gtc gtg tcc acc caa ctg ctc ctg aat ggc tcc ctg	IKPVVSTQLLLNGSLAEEEIIIRSENLTNN R	y v v v v v v v v v v v v v v v v v v v

FIGURE 12 (Cont)

A E E E I I I R S E N L T N N A K T I I V H L N E S V E I N (V) Q K V get gag gaa gat rit ric att agg tee gag aat yte aca rac aat gye aaa acc att ate gie cam ete aac raa age gie gwg att aac A K T I I V H L N E S V E I N C T R P N N T R K V V S and acc at gtg caw ctg aat rag tcc gtg gwa atc aat tgc aca agg cct arc aat aac aca agg ama

Segment 6

Segment 1

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Segment 3

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YKVVKIEPLGVAPTRAKRRVVERKKR EKI tac aaa gtg gtc raa atc raa ccc ctc ggc rtt gcc cct acc ara gcc aaa agg aga gtg gtc sag aga gag aaa agg

ara gac aat tgg aga agc gaa ctg tat aag tat aag gtc gtg rag att rag cct ctg gga rtc

ggc rat ats ΩZ

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GAP IN SEGMENTS DUE TO HYPERVARIABLE REGIONS 3,4 AND 5

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Segment 4		Segment 5		Segment 6	
FGFLGAAGSTMGAASITLTVQA	Γ Γ Γ In mtc gga gc Γ	AASITLTVQARQLLSGIVQQQSNLL	gga agc aca atg gga gcc gct agc atk acc ctc acc gtc cag gct agg cwa ctg ctc agc gga atc gtc cag caa cag arc aat ctg ctc	GIVQQQSNLLRAIEAQQHLLQLTVW	L) aga cwg ctc ctg tcc ggc att gtg caa cag caa art aac ctc ctg agg gct atc gaa gcc caa cag cat mtg ctc cag ctc acc gtc tgg
Ŋ	c 99a	T W	9 99	ഗ	g to
A V G I	ᆲ	Σ	a atí	디디	i O Č
ט	9 99a	€	9 0		g GČ
>	gct gtg	ß	agc 1	O,	⊒ Š̃
Ø	gct	Ŋ	gga	ĸ	aga

Segment 7		Segment 8		Segment 9	÷	Segment 10	:	Segment 11	Segment 12)
RAIEAQQHLLQLTVWGIKQLQARVLAVERY M	aga gcc att gag gct cag caa cac wig cig caa cig aca gig igg ggc att aag caa cig caa gcc aga gig cic gcc rit gag aga tac		gga atc aaa cag ctc cag gct agg gct rtc gaa agg tat ctg aaa gac caa mag γ tt ctg gga mtc tgg ggc tgt agc gga aag	ICTTAVPWNS	ytc ctc ggo	W S N K S L E	S L E E I W N M T W M E W E R E I S N V T N	IQ SL K g aca tgg atk sag tgg gag aga gag att agc aat tac aca arc cwa atc tat rag att	QIYEILTE	${ m K}$ ${ m D}$ gaa agg gaa atc tcc aac tat acc art cwg att tac raa atc ctc acc gaa agc caa aac caa cag gat agg aat gag maa gaa ctc ctg
						•				

Segment 13	Segment 14	Segment 15	Segment 16	Segment 17	Segment 18
TESONQODRNEQELLLELDKWASLWWWFDIT KDA aca gag tcc cag aat cag caa gac aga aac gaa mag gam ctg ctc gmg ctc gac aaa tgg gct agc ctc tgg aat tgg ttt rac att asc	ELDKWASLWWFDITNWLWYIKIFIMUGGGGAAN SKA A SLWWBGAAL 1999 AAC 1999 AA	N W L W Y I K I F I M I V G G L I G L R I V F A V L S I V N K V I I I S to ato ato ato ato ato ato ato ato ato	LIGLRIVFAVLSIVNRVRQGYSPLSFQTLLL V ctc rtc gga ctg aga atc rtt ttc gct gtg ctc agc att rtc aat agg gtc agg caa ggc tat agc cct ctg tcc ttc caa acc ctc myc	RVRQGYSPLSFQTLLPAPRGPDRPEGIEEEF T aga gtg aga cag gga tac tcc ccc ctc agc ttt cag aca ctg myg ccc gct ccc aga ggc cct gac aga cyc gra sgc att gag gaa gag	PAPRGPDRPEGIEEEGGEQDRDRSVRLVSG LGR RGG N

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Segment 19	Segment 20	Segment 21	Segment 22	Segment 23	Segment 24
GEQDRDRSVRLVSGFLALAWDDLRSLCLF RGG a ggc gaa crg grt agg grt agg tcc gtg aga ctg gtc arc gga ttc tya gcc ctc gcc tgg gac gat ctg aga arc ctc tgc ctc ttc	LALAWDDLRSLCLFSYHRLRDLILIAARI S t tyg get etg get tyg gat etg ag art etg tyt etg ttt age tat eac aga etg aga gac ytt atc etc ate gyt gee aga aye	YHRLRDDDILIAARIVELLGHSSLRGLRRG.ctac cat agg ctc agg gat ytc att ctg att gyc gct agg ayt gtg gaa ctg ctc ggc ctt agc tcc ctg ara ggc ctc crg aga ggc	ELLGHSSLRGLRRGWEALKYLWNLLQYWG R K Q G WG L	EALKYLWNLLQYWGQELKISAVSLLNATA G WG L L L L 19 gag gst ctg aaa tac tkg kgg aat ctg ctc cwg tac tgg ggc cwg gaa ctg aaa awc tcc gcc rtt agc ctc ctg aat gcc aca gcc	ELKISAVSLLNATAIAVAEGTDRVIEVAQ , ,a gag ctc aag awt agc gct rtc tcc ctg ctc aac gct acc gct atc gct gtg gct grg kgg acc gat agg rtt atc gaa gtg gyt cag
ධ gga	رد 1 م در 1	ကို လ	V	₩ 199	Q L S

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Segment 25		Segment 26		
	gac aga rtc att gag gtc gyc caa agg gct kgg aga gcc att ctg mat atc cct asa aga atc aga cag	ROGLERALL		mac att ccc asg agg att agg caa ggc ytt gag aga gcc ctc ctg
Q R A G	caa agg gct kgg	QGLE	ഥ	caa ggc ytt gag
∢ >	tc gyc	ద		tt agg
>	ag g	R H		9g a
Ю	tt g	저		නු ය
H	tc a	ρς,	[-	ю СС 3
> H	gar	БР		ָנָר נ
<u>к</u>	ac a		1 -2	ac a
D D	aca g	끄	Z	tc =
r O ≥	e 56	Н		atc c
in the	yra k	<		gct a
	300	۲2 ا		999
	atc (ט	Z	663
A V A) သင်			300
Н	att gcc gtc gcc gra kgg	R A		aga gcc kgg agg gct atc ctc

NEF OVERLAPPING SEGMENTS

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			33/210		
Segment 1	Segment 2	Segment 3	Segment 4	Segment 5	Segment 6
GKWSKSSLVGWPEVRERIRQTPPAAEGV CPPA99c aaa tgg tcc aag wgc tcc cyc gtc gga tgg ccc gma gtg aga gag aga atc aga crg rca acc cct gcc gct gag gga gtg	ERIROTPPAAEGVGAVSQDLDKHGAITS RAA 9 988 agg att agg cra rcc gct gcc gaa ggc gtc ggc gct gyc tcc crg gat ctg gat aag kac gga gcc mtc acc tcc	VSQDLDKHGAITSSNTPANNADCVWLKAA PRSQC SCT GCC ast acc sct gcc ast acc sct gac tgt gyc tgg ctc rag gct	NTPANNADCVWLKAQEEEGVGFPVRPQVP A E E	EEEGVGFPVRPQVPLRPMTYKGAFDLSFF B gag gaa gag grc ggc ttc ccc gtc agg cct cag gtc ccc ctg aga cct atg acc tac aaa gaa gcc rtc gat ctg tcc ytc ttc	LRPMTYKGAFDLS(F)FLKEKGGLEGLVYSKK AVL otc agg occ atg aca tat aag gac get rtt gac otc agc ytg ttt ctg aaa gag aaa ggc gga ctg gaw ggc otc rtc tat agc mag aaa
M G atg gga	V R gtc agg	G A	S N agc aa	Cas gar	L R

Segment 7

S K K R Q E I L D L W V Y H T Q G $\stackrel{F}{(Y)}$ Q N Q D N N $\stackrel{V}{(Y)}$ tcc maa aag agg caa gas att ctg gat ctg tgg gtg tat mac aca cag gga twc

L K E K G G L E G L

D

ctc aag gaa aag gga ggc ctc gas gga ctg

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cag gaw atc ctc gat ctc tgg gtc tac mat acc caa ggc twt ttc cct gac tgg cas aat tac aca ccc gga ccc gga ryc aga tac

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	56/2	16			
Segment 9		Segment 10		Segment 11	
DWHNYTPGPGIRYPLTFGWCFKLVPVDP Q V	ccc gat tgg caw aac tat acc cct ggc cct ggc rya agg tat ccc ctc acc ttt ggc tgg tgc ttt aag ctc gtg cct gtg gat ccc	TFGWCFKLVPVDPREVEEINKGENNCLL S A E	ctg aca ttc gga tgg tgt ttc aaa ctg gtc ccc gtc gac cct ags gaa gtg gaa gag ryc aac raa ggc gaa aac aat tgc ctc ctg	VEEINKGENNCLLHPMSQHGMEDEEREV A E	gtc gag gaa ryc aat
Ω	ដ	H	ŭ	田	w gag

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FIGURE 12 (Cont)

Segment 12	1		Segment 13
ø		itg gag gat gag gaw agg gaa gtg ctg awa tgg aaa ttc gat agc crt ctg gct ckc agg cat ats gct	
н	Σ	t at	
耳		g G	
ഷ		g D	t
EEREVLIWKFDSRLARRHIA	Ц	טֿ ע	RLARRHIARELRPEFYKDC H L M H Y
Þ		90	A S
П		n Cţ	×
മ	H	O	>
ഗ		t ag	LRPEFYKD H Y
Ω		n ga	(H)
Ŀ		a tt	<u>а</u>
×		g a	ᅜᄪᅧ
3		a tg	H ;
Н	×	ığ ığ	LARRHIARE L M
П		9 Ct	24
>		a gt	4 5
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	ATC/ATT		ATS/ATK AWC/AWT WTC/WTT AKA/ MTC/MTT AKC/AYT	AWA
	I Ile		IN I	H
	CAC/CAT		MAC/MAT SAC/SAT CAM/CAW CRC/CRT CWC/CWT	
	н Нів	cids	H H H H H H H H H H H H H H H H H H H	
	G Gly GGC/GGA	Amino A	KGG/ GRC/GRT GRG/KGT GRG/GRA GSC/GST SGC/RGA RGC/GRC	
	G Gly	More	99 99 99 99 99 99 99 99 99 99 99 99 99	5
	GAA/GAG	TWO OF	GAS/GAM SAG/SAA GMG/GMA GRG/GRA RAG/RAA GWG/GWA	
	E Glu	For	ED ES	
	CAG/CAA	Codons	CRG/CRA SAG/SAA CAM/CAW CWG/CWA MAG/MAA	
**	o o u o	erate	98 99 99 99	
d Codons	TGC/TGT	d Degene	TCS/TCK YGC/YGT KGC/KGT TKC/TKT WGC/WGT	
Use	cys	Use	3888888	
Most Frequently Used Codons	D C C ASP GAT CYS TGC/TGT GIN CAG/CAA	Most Frequently Used Degenerate Codons For TWO or More Amino Acids	RAC/RAT GMC/GMT GAS/GAM GRC/GRT SAC/SAT KAC/KAT	
it Fr	D Asp	st Fr	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
	N Asn AAC/AAT		NA RAC/RAT MAC/MAT AMS/AMM ARS/ART AMC/ART WAC/AMT	
s pue	N Asn	and 8	SITIC ND NH NI NK NS NT	
First	AGG/AGA	First	NGLE PO: AKT/ WGG/YGG YGC/YGT CRG/CRA CRC/CRA ARG/ARA AKA/	SGC/RGA CSC/CST ASA/ASG CKG/CKC MGC/MGT
Code-	R Arg	-apop	A SI RW RC RO RR RH RK	RG RT RL RS
The Genetic Code- First and Second	GGC/GCT	The Genetic Code- First and Second	BASES AT A SINGLE POSITION GMC/GMA RW WGG/YGG NH P GCC/GST RC YGC/YGT NI P SCC/SCT RQ CRG/CNA NK P KCC/KCT RH CRC/CRI NS P CCC/RCT RH CRC/RT NT P GYC/RCT RH CRC/RT NY P GYC/GYT RI ARA/ NY P	
The	A Ala	The	TWO ABB ABB ABB ABB ABB ABB ABB ABB ABB AB	

FIGURE 13

Single letter code

R = A or G

Y = C or T

K = G or T

S = C or G

W = A or T

H = A or C or T

U = A or C or T

N = A or C or T

A or C or G

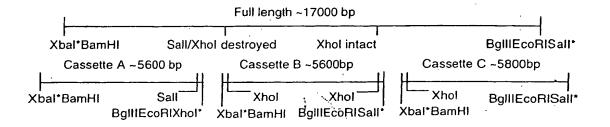
D = A or C or G

The Genetic Code- First and Second Most Frequently Used Codons

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	cre/crc			MYG/WTG	TKG/	TYG/TYA	CWG/CWA	ر ارا ارا	YTC/YTT	MTC/M	C/C/	STG/S1	CKG/C						_	_					
	r Leu			Ξ	3	ĽS	3	3	<u>ن</u> د	3	c	Υ.	ጟ												
	GTG/GTC			RTG/	GWC/GWT	GWG/GWA	KTC/KTT	RTC/RTT	GYC/GYT	פאפיינאר	STG/STC		٠												
	v Val	cids		₹	8	ΛE	ا <u>د</u>	7	٠ ا	2	7														
	Y Tyr TAC/TAT	TWO or More Amino Acids		WAC/WAT	KAC/KAT	TRC/TRT	YAC/YAT	IWC/IWI	TMC/TMT																
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	TGG/			WGG/YGG	KGG/	TSG/	TKG/	165/16K																	
	¥ Trp	For		WR	¥G	S.		¥																	
	T Thr ACC/ACA	e Codons		AYG/	AMC/AMT	AMG/AMA	AYC/AYT	ACC/ RC 5	ASA/ASG	,															
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	AGC/TCC	Most Frequently Used Degenerate Codons For		TSG/	ARC/ART	TYG/TYA	TOW/COM	TAT/ 171	AKC/AKT	100/000	RCC/RCI	KGC/ KGT	ASC/WCC	MGC/MGT											
,	r Ser	tly u		SW	SN	SI	2 6	, ,	, r.	; ;	X 0	ָה מ	ST	SB											
•	טטנ/טט	Frequen		CMG/CMA	CMC/CMT	SCC/SCT	נאני/נאני) () () () () () () () () () (MCC/MCT	9															
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	Phe	and	OSITI	FC	FI	1 6	2 5	: 2																	
	ATG/	- First	INGLE P	AKT/	ATS/ATK	MIG/WIG	\0\d) UE &	2						de										or T
	₩ Wet	Code	T A S	AR	Σ	ž Ž	4 E	£	:						er cc						or T		or G		or G
	AAG/AAA	Genetic Code- First and Second	TWO BASES AT A SINGLE POSITION	AWG/	AAS/AAM	MAG/MAA	ARG/ARA	AMG/AMA	AWA						Single letter code	A or G	C or T	G or T	C or G	A or T	A or C	CorG	A or C	A or G or	Ø
	K Lys	The	TWO	₹	₹ 9	Ş.	2 2	Ţ	T						Sing	n ex	Y	×	S	3	n =:	e CO) -	Ω	l) Z

FIGURE 13 (cont)



Full length construction after cloning the cassettes into pBS-Sites marked with a "*" are in the pBS MCS

Cassette Extras (Can be removed from cassette ends)

A (37bp) BamHl/Kozak Start	Sall Stop Bglll EcoRl
5' gc ggatccacc atg	gtcgac tga agatct gaattc gc 3'
B (43bp) BamHl/Kozak Start Xhol	Xhol Stop Bglll EcoRl
5' gc ggatccacc atg ctcgag	
C (37bp) BamHl/Kozak Start Xhol	Stop Bglll EcoRl
5' go goatceaco ato ctogad	tga agatet gaatte gc 3'

FIGURE 14

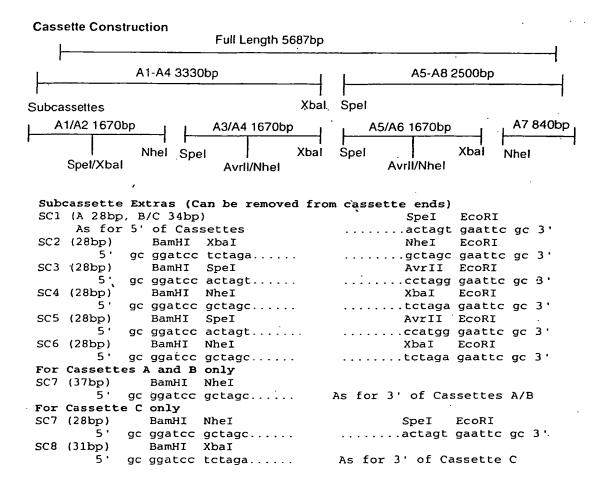
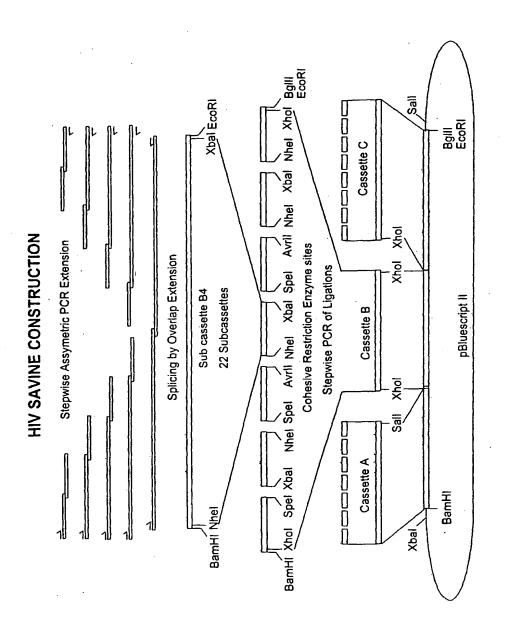


FIGURE 14 (Cont)



TIGURE 14 (Cont)

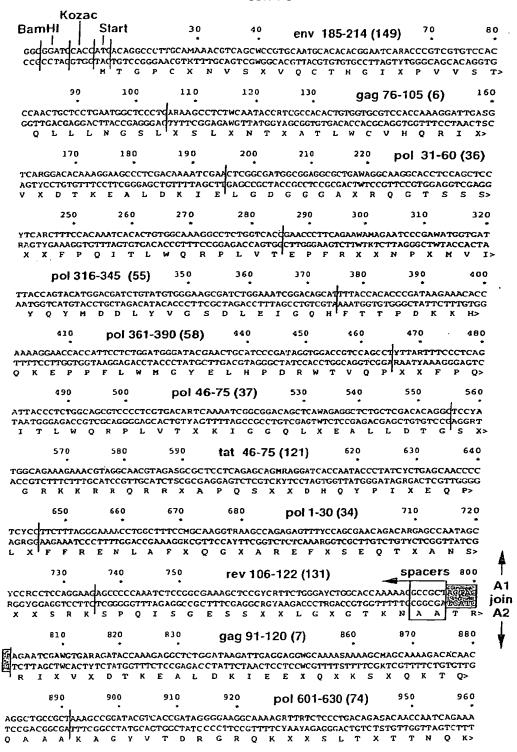


FIGURE 15

970	980 99	0 1000	1010	env 4	6-75 (140)	1040	
•	• 1	•					
ACCGAACTGCAWG	CCATTCAMGAMGCCRM	TACCACACTGTT	PTGCGCCAGCG.	ATGCCAAAGC	CYATGASACAG	AGGICCA	
TGGCTTGACGTWC	GGTAAGTKCTKCGGYK.	ATGGTGTGAC AA	AACGCGGTCGC	TACGGTTTCG	GRTACTSTGTC	TCCAGGT	
TELX	XAXX	TTLF	CASI	DAKA	ххт	E V H	>
1050	1060 1070	0 1080	1090	pol 76	6-105 (3 9)	1120	
•		* ,	•	•		*	
CANTCTCTCCCCC	ACACACGCTTGCGTCCC	COCTGACGATAC	AGTGCTGGAGG	CASATSAACC	TCCCCGGAARA	TGGAAGC	
COMPACACACCCCCC	POTETECCA ACCCA GGC	cdccactgctat(TCACGACCTCC	TSTASTIGG	AGGGGCCTTY T	ACCTICG	
GIIACACACCCC.	T H A C V I	ADDT	VLE	X X N	LPGX	W K>	
14 4 11 11							
1130	1140 1150	1160	1170	1180	1190	1200	
1130	1140 1150	*	•	•	• ,	•	
	GGAATCGGCGGATTCA	man v conce caja	PCATCGGACCC	TOOSAAAS	PACAATACCCC	ARTCTTC	
CTAAGATGATTGG	CCTTAGCCGCTAAGD.	NAMEGICACITY	VCTACCCTGGG	CTTTTCGGA	TGTTATGGGG	TYAGAAG	
GATICTACTAACCC	G I G G F	ANTICCACICAL	Y T C P	F N P	V N T P	X F>	
PKMIG	GIGGF	IKVK	x 1 0 .	<i>D</i>			
			1250	1260	1270	1280	
pol 196-22	25 (47) 1230	1240	1230	1200			
•				₩ ₽₩₩₩₩₩₩	· > > W > TO CTO TO	ACCAAAG	
GCTATCAAGAAAA	GGACTCCACCAAATGG	AGAAAGCTCGTG	GATTTCAGART	INGGALIATO	TO COLUMN TO COL	CCTTC	
CGATAGTTCTTTT	CCTGAGGTGGTTTACC	TCTTTCGAGCAC	CTAAAGICITA	AICCIANIA	Y T Y	, u e>	
AIKKK	D S T K W	RKLV	D F H.X	K I I	X 1 L .	. 0 3-	
				1240	1350	1360	
1290	rev 16-45 (125)	1320	1330	1340	1350	1360	
•	• •	• _				PTACCC	
CAATCCCTATCCTA	GCTCCGAAGGCWCCAG	GCAARCCAGAAR	GAATAGGAGAA	GGAGATGGGG	MGGC GAMC RGC	N I AGGG	
OFFINE COCKETS CONT	このかにないてすべいに紹にらずく	CCTTYCGTCTTY	CTTATCCTCTT	CCTCTACUCC	1006011610	INICCC	
NPYP	S S E G X R	QXRX	NRR	R R W'G	GEX	X R>	
	ì					1440	
1370	1380 env 52	25-554 (171)	1410	1420	1430	1440	
• .		• • •		•			
ATAGGTCCGTGAGA	CTGGTCARCGGATTCT	YAGCCCTCGCCTC	GGACGATCTG	AGAARCCTCT	GCCTCTTGGAM	MACCTC	
THE PROPERTY OF THE PROPERTY O	へんべんれんせいさんしてあるほと	RTCGGGAGCGGA(CCTGCTAGACT	ICTTYGGAGA	COCNONNACIV	1 1 GGAG	
D R S V R	L V X G F	XALAV	N D D · L	RXL	C L F'X	N L>	
5 1. 15							
1450	1460 1470	env 31-	60 (139)	1500	1510	1520	
	• •			•	• 1	•	
TGGGTCACCGTCTAG	TATGGCGTCCCCGTCT	PGGAGAGASGCTF	MCACAACCCTC	TTCTGTGCC'	ICCGACGCTAA	GGCTYA	
	~ * ** * * * * * * * * * * * * * * * *	、 たたかへかくからしに みり	KCTCTTGGGAG	AAGACACGG	ACCULTUCEAL:	CCGMMI	
WVTVY	Y G V P V	WRXA	X T T L	FCA	SDAK	A X>	
			*				
spacers	1550	1560	rev 1-30	(124)	1590	1600	
	•	•			•	•	
decreed Teerre	CAGAAGCGGCRRCACA	GACGAAGAGCTC	CTGARGGCTRT	CAGAATCAT"	TAASATTCTGT	ATCAGT	
decadedeaceare	·C·rC·T·T·C·C·CC·C·C·YC·T·C·T	``TGCTTCTCGAG	GACTYCCGAYA	GTCTTAGTA	ATTSTANGACA.	TAGTCA	
A A M A C	RSGXT	DEEL	LXAX	RII	XIL	Y Q>	A
	,						4
1610	1620 1630	1640	1650	vif 16-4	5 (101)	1680	- 1
			•		•	*	A2
	CCCCTAGTATGARAAT	тась асст сс а а	SAGCCTGGTCA	AGCATCACAT	GYACATCTCC/	AAGAAA	AZ
CAACCCTTACCCTT	GOGGATCATACTYTTA	CIPCTTGGACCTT	STEGGACEAGT	TCGTAGTGT	CRTGTAGAGGT	TTTTT	join
GGTTGGGAATGGGAA	GCGGWAGNI WC 1 1 1 1 W	RTWX	S 1. V	к н н в	XIS	K K>	A3
5 N P Y P	SASMXI	K 1 14 V	3 D V	•. •			- 10
			1770	1740	1750	1760	- 1
1690	1700 1710	1720	1730	1/40	1.50		¥
*	•				·		4
SCCAAWGGCTGGTTC	TATAGGCATCACTWTG	ASGAGTCCGAGS	TCGTGARTCAG	ATTATCGAAV	AGCTCATCAAA	WAGGA	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	`ATATCCCTACTCAWAC	TSCTCAGGCTCS	AGCACTYAGTC	TAATAGCTTE	LICCACIACI I	TICCI	
AXGWF	Y R H H X	XESE	X V X Q	IIE	XLIK	K E>	
1 CC4 CO0	(78) 1790	1800	1810	1820	1830	1840	
				•	•	•	
	ATGGGTACCAGCCCAC			GCTCCAGAAM	CAGATTMYCAA	COTRAL	
AARGGTCTACCTAKC	TACCCATGGTCGGGTG	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	ℂℸ⅌⅌ℂℂℼℼℼℂℼ	CGAGGTCTTK	GTCTAAKRGTT	TTAGG	
<b>PTYCCAGATGGATM</b> G	TACCCATGGTCGGGTG	1 ICCC I TAGCC T		1 0 2	O T X H	( T>	
XVYLX	W V P A H	K G I G	QTKE	P 7 V	A		
						1920	
1850	pol 916-945 (95)	1880	1890	1900	1910	1 250	
			* 1	•	•		
, <u>, , , , , , , , , , , , , , , , , , </u>	ACTATAGGGATAGCAG.	AGACCCTMTCTG	GAAGGGACCGA	<b>AAAGCYTTGA</b>	GGAAATCTGGR	RACAAT	
OPPORTUGATION AND COCCAGA	TICATATICCCTATCGTC	TCTGGGAKAGAC	こてすこくこていらばすず	TTTCGRAAC'I	CCLLINGACCI	TGTTA	
ITITI GAAATUUC AGA	Y Y R D S R	D D V III	K C 27'	K S X F	EIW	X N>	
		1/ P A W	N () F (				

FIGURE 15 (Cont)

env 405-434 (163) 1960 1970 1980 1990 2000 ATGACATGGATKSAGTGGGAGAGAGAGATTAGCAATTACACAARCCWAATCTATRAGATTCTCARACCCGAACCCACAGC TACTGTACCTAMSTCACCCTCTCTCTCTCAATCGTTAATGTGTTYGGWTTAGATAYTCTAAGACTYTGGGCTTGGGTGTCG
M T W X X W E R E I S N Y T X X I Y X I L X P E P T A> 2050 2010 2020 2060 2070 2080 gag 451-480 (31) CCCTCCCGCTGAGARTTTCGGTTGGGTGAGGAAACTACACCCTCCCHAAAGCAAGAGCHAAAGGATAAGGACAATACG GGGAGGGCGACTCTYAAAGYCTAAGCCACTCCTTTGATGTGGGAGGGKTTTCGTTCTCGKTTTCCTATTCCTGTTATGC PAEXFXFGEETTPSXKQEXKDKE[†] 2090 2100 2110 pol 106-135 (41) 2150 2160 ATCAGATTHTTATTGAGATTTGCGGCAAGAAAGCTATTGGTACAGTGCTCGTGGGACCTACCCCTGTGAATATCATTGGCTAGTCTAAKAATAACTCTAAACGCCGTTCTTTCGATAACCCATGTCACGAGCACCCTGGATGGGGACACTTATAGTAACCG D Q I X I E I C G K K A I G T V L V G P T P V N I I G> 2170 2180 2190 2200 vpr 46-75 (115) 2230 agaatttacgaaacctatggcgatacctgggagggcgtcgaggctctgatcagaaycctccagcaactgmtgtttrtcca TCTTAAATGCTTTGGATACCGCTATGGACCCTCCCGCAGCTCGAGACAATAGCTCTTRGGAGGTCGTTGACKACAAAYAGGT I-Y E T Y G D T W E G V E A L I R X L Q Q L X F X H> 2270 2280 2290 tat 31-61 (120) TTTCAGAATCGGAPGTTWTCATTGCCAASTGTTTTTCTCACCAAAGGTCTCGGCATTAGCYACGGAAGGAAAAAGAGAA AAAGTCTTAGCCTACAAWAGTAACGGTTSACACAAAAGAGTGGTTTCCAGAGCCGTAATCGRTGCCTTCCTTTTTCTCTT F R I G  $^{\circ}$  C  $^{\circ}$  H C  $^{\circ}$  Q X C F  $^{\circ}$  L T K G L G I S X G R K K R> 2340 spacers 2370 2380 tat 1-30 (118) 2330 RACAGAGAGGGGGGGCTCCCCAGCTGCCCATGGACCCCGTGGACCCCCASCTGGAGCCTTGGAWCACCCTGGCTCCCAG YTUTCTCTTCSCTCGAGGGGTTCGACGGTACCTGGGGCACCTGGGGTTSGACCTCGGAACCTTWGTGGGACCGAGGGTC X Q R R X A P Q A A M D P V D P X L E P W X H P G S Q> 2440 2450 2460 2470 2420 CCTAMGACAGCCTGTWMCAAATGCTATTGCAAAAAGTGGGTAGGGAAGAGACAACCCCTAGCCMGAAACAGGAACMGAAGGATKCTGTCGGGACAWKGTTTACGGTAAACAGGTTTTTCACGGGAEGGCTTCTCTTGTTGGGGATCGGKCTTTGTCCTTGKCTT ΑЗ join PXTACXKCYCKKC EETTPSXKQEXK> A4 2520 . 2510 gaq 466-495 (32) AGACAAAGAACWCTACCCCCCTTYAGCCAGCCTCAAGTCCCTGTTTGGCAATGAGAATTTCAATATGTGGAAGAATRACA
TCTGTTTCTTGWGATGGGGGGAARTCGGTCGGAGTTCAGGGACAAACCGTTACTGTTAAAGTTATACACCTTCTTAYTGT
D K E X Y P P X A S L K S L F G N D N F N M W K N X> 2620 2570 2600 2610 env 91-120 (143) TGGTGGAMCAGATGCAMGAAGACRITATCTCACTATGGGACCAAAGCCTCAAGCCTTGCGTCAAGCTCGACGTCGGCGAT ACCACCTRGTCTACGTRCTCTGYAATAGAGTGATACCCTGGTTTCGGAGTTCGGAACGCAGTTCGAGCTGCAGCCGCTA
M V X Q M X E D X I S L W D Q S L K P C V K L D V G D> 2650 2660 pol 256-285 (51) 2690 2700 2710 2720 GCCTATTTCTCCGTGCCTCTGGATRAARRCTTCAGAAAGTATACCGCTTTCACAATCCCTAGCAYAAACAATGAGCAACT CGGATAAAGAGGCACGGAGACCTAYTTYYGAAGTCTTTCATATGGCGAAAGTGTTAGGGATCGTTTTGTTACTCGTTGA
A Y F S V P L D X X F R K Y T A F T I P S X N N E Q L> 2730 2740 2750 2780 pol 751-780 (84) CTTTCCGCTTCGGTASGTACCGGTTCACYTAACGAGTGGTCCGTAAACCGTTGACCTAACGTGTGGGACCTCCCTTTCY K G E A X H G Q V X C S P G I W Q L D C T H L E G K> 2820 2830 2840 2810 pol 166-195 (45) TTATCCTAAGGTCAAGCAATGGCCTCTGACAGAAGAAAAGATTAAGGCTCTGACTGHGATTTGCAMAGAGATGGAGVAA 

FIGURE 15 (Cont)

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**A5** 

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2910 2940 2950 2960 2890 2900 pol 331-360 (56) GAGGGAAAGATTAGGATGACCTCTACGTCGGCTCCGACCTGGAGATTGGCCAACATAGGRCCAAAATCGAAGAGCT CTCCCTTTCTAATCGTACCTGAGATGCAGCCGAGGCTGGACCTCTAACCGGTTGTATCCYGGTTTTAGCTTCTCGA E G K I S M D D L Y V G S D L E I G Q H R X K I E E L> 3030 2990 3000 2970 2980 pol 616-645 (75) CAGGSMACACCTCCTGARATGGGGGCTCACCGAMACCACAAAACCAAAAGACTGAGCTCCAMGCTATCCAWCTGGCTCTGC GTCCSKTGTGGAGGACTYTACCCCTGAGTGGCTKTGGTGTTTGGTTTTCTGACTCGAGGTKCGATAGGTWGACCGAGACG
R X H L L X W G L T X T T N Q K T E L X A I X L A L> 3090 3070 3080 3060 3050 pol 796-825 (87) AAGACTCCGGCTYAGAGGTCAACATTGTGACAGAdATTCCCGCTGAGACTGGTCAAGAGACCGCCTATTTCHTTCTGAAA TTTTGAGGCCGARTCTCCAGTTGTAACACTGTCTCTAAGGGCGACTCTGACCAGTTCTCTGGCGGATAAAGKAAGACTTT Q D S G X E V N I V T D I P A E T G Q E T A Y F X L K> 3200 3170 3180 3190 3150 3160 3140 CTGGCTGGCAGATGGCCTGTGARARYCATTCACACAGACAATGGGAGGACAAAGATTGAGGAACTGAGASMGCATCTGCT GACCGACCGTCTACCGGACACTYTYRGTAAGTGTGTCTGTTACCCTCCTGTTTCTAACTCCTTGACTCTTSKCGTAGACGA
L A G R W P V X X I H T D N G R T K I E E L R X H L L> 3270 3250 3260 3230 3240 pol 346-375 (57) WGFTTPDKKHQKEPPFLSS 3330 spacers 3320 3290 vif 166-192 (111) ATARGTGGAACRAACCCCAGAAAAYCAAGGGACRCAGAGRAAATCACACAATGAATGGCCATGCTGCCACAGAGTCCCAG TATYCACCTTGYTTGGGGTCTTTTRGTTCCCTGYGTCTCYTTTAGTGTGTTTACTTACCGGTACGACGGTGTCTCAGGGTC D X W N X P Q K X K G X R X N H T M N G H A 3420 env 435-464 (165) 3410 3370 AATCAGCAAGACAGAAACGAAMAGGAMCTGCTGGMGCTCGACAAATGGGCAAGCCTCTGGAATTGGTTTRACATTASCSA TTAGTCGTTCTGTCTTTGCTTKTCCTKGACGACCKCGAGCTGTTTACCCGTTCGGAGACCTTAACCAAAYTGTAATSCTT N Q Q D R N E X X L L X L D K W A S L W N W F X I X D 3510 3520 3500 3470 3450 3460 gag 121-150 (9) CACCGGAARTAGCTCCMAAGTGTCCCAGAATTACCCTATCGTCCAGAATSYCCAAGGCCAAATGGTCCACCAASCCMTCT GTGGCCTTYATCGAGGKTTCACAGGGTCTTAATGGGATAGCAGGTCTTASRGGTTCCGGTTTACCAGGTCGTTSGGKAGA T G X S S X V S Q N Y P I V Q N X Q G Q M V H Q X X> 3600 3560 3550 env 480-509 (168) 3540 3530 3630 3640 3650 3620 vif 106-135 (107 3610 TCCTTCCAAACCCTCMYCTCATCCATCTGYAWTACTTTGACTGTTTCKCTGACTCCRCCATTAGGAGAGCCATCCTGGG aggaaggtttgggagkrqgagtaggtagacrtwatgaaactgacaaagmgactgaggyggtaatcctctcggtaggaccc S F Q T L X L I H L X Y F D C F X D S X I R R A I L G> 3720 3730 3700 3710 acasakagtgagmaggagatgcgaayadgctg1gggamtcggagccatgwtcy1tggctttctgggtgccgctggctcca TGTSTMTCACTCKTCCTCTACGCTTATCCGACACCCTKAGCCTCGGTACWAGRAACCGAAAGACCCACGGCGACCGAGGT X X V X R R C E Y A V G X G A M X X G F L G A A G S> 3830 3790 3610 env 300-329 (156) CCATGGGCGCTGCCTCCATSACACTGACAGTGCAAGCCTATCACCCTAGCAAAGACCTCRTTGCTGAGATTCAGAAACAG GGTACCCGCGACGGAGGTASTGTGACTGTCACGTTCGGATACTGGGATCGTTTCTGGAGYAACGACTCTAAGTCTTTGTC
T M G A A S X T L T V Q A Y D P S K D L X A E I Q K Q>

PHENNE 15 (Cont)

pol 466-495 (65) 3870 3880 3890 3900 3910 3920 GGTCAGGRTCAGTGGACATWTCAGATTTWCCAAGAGCCTTTCAAAAAdGGAACCGTCCTGGTCGGCCCTACACCCCGTCAA CCAGTCCYAGTCACCTGTAWAGTCTAAAWGGTTCTCGGAAAGTTTTTCCTTGGCAGGACCAGCCGGGATGTGGGCAGTT

G Q X Q W T X Q I X Q E P F K N G T V L V G P T P V N> 3960 3970 3930 pol 121-150 (42) CATCATCGGAAGGAACHTGCTGACACAGHTTGGCYGCACCCTCAACTTTCCCATTAGGAAAGGCAGCCCTGCTATCTTTC
GTAGTAGCCTTCCTTGKACGACTGTGCKAACCGRCGTGGGAGTTGAAAGGGTAATCCTTTCCGTCGGGACGATAGAAAG
I I G R N X L T Q X G X T L N F P I 5 K G S P A I F> 4070 4050 4060 4080 4010 4020 pol 301-330 (54) AGTCCAGCATGMCAMAGATTCTGGAGCCTTTTAGGAWAMAAAACCCTGASATGGTCATCTATCAGTATEGTAGGCCTCTC TCAGGTCGTACKGTKTCTAAGACCTCGGAAAATCCTWTKTTTTGGGACTSTACCAGTAGATAGTCATA Q S S M X X I L E P F R X X N P X M V I Y Q Y 4090 4100 . 4110 nef 136-165 (188) 4140 4150 ACATTCGGATGGTGTTTCAAACTGGTCCCCGTGGACCCCAGSGAAGTGGAAGAGRYCAACRAGGGCGAAAACAATTGCCT TGTAAGCCTACCACAAAGTTTGACCAGGGGCACCTGGGGTCSCTTCACCTTCTCYRGTTGYTCCCGCTTTTGTTAACGGA T F G W C F K L V P V D P X E V E E X N X G E N N C L> 4200 4190 pol 271-300 (52) CCTQTTTAGGAAATACACAGCCTTTACCATTCCCTCCAYCAATAACGAAACCCCTGGCATTAGGTATCAGTATAACGTCC GGAQAAATCCTTTATGTCTCGGAAATGGTAAGGGAGGTRGTTATTGCTTTGGGGACCGTAATCCATAGTCATATTGCAGG FRKYTAFTIPSXNNETPGIRYQ 4260 4270 4280 4290 env 315-344 (157) 4250 TGCCTCAGGGATGGGGAAGCACAATGGGAGCCGCCAGCATKACCCTCACCGTCCAGGCTAGGCWACTGCTCAGCGGAATC ACGGAGTCCCTACCCTTCGTCTTACCCTCGGCGGTCGTAMTGGGAGTGGCAGGTCCGATCCGWTGACGAGTCGCCTTAG L P Q G W G S T M G A A S X T L T V Q A R X L L S G I> 4360 4370 pol 451-480 (64) 4350 4330 4340 GTCCAGCAACAGARCAATCTGCTGGGGGGGAGAATAGGGGAAATCCTCARAGAGCCTGTGCATGGCGTCTACTACGATCCCTC CAGGTCGTTGTCTYGTTAGACGACKCCTCTTATCCCTTTAGGAGTYTCTCGGACACGTACCGCAGATGATGCTAGGGAG VQQQXNLLXENREILXEPVHGVYYDPS 4450 4480 4410 4440 vpu 61-81 (136) spacers 4510 4520 4530 vpr 61-90 (116) GAGTGGACAATAACCTGCCCCTATTAGAAYCCTGCAACAGCTCHTGTTCRTTCACTTTAGGATTGGCTGCCRGCACTCC CTCACCTGTTATTGGACGGCGATAATCTTRGGACGTTGTCGAGKACAAGYAAGTGAAATCCTAACCGACGGYCGTGAGG G V C N N L A A I R X L Q Q L X F X H F R I G C X H S> 4570 4580 4590 4 600 4610 gag 406-435 (28) AGGATTGGCATCMYCCGTCAGAGAAGGGSCAGAGCTCCCAGGAAAAAGGGATGCTGGAAGTGTGGCARAGAGGGACACCA TCCTAACCGTAGKRGGCAGTCTCTTCCCSGTCTCGAGGGTCCTTTTTCCCTACGACCTTCACACCGTYTCTCCCTGTGGT R I G I X R Q R R X R A P R K K G C W K C G X E G H Q> 4670 4680 4690 4700 4650 GATGAAGGATTGCACTGAGAGACAGGCTAACTTTCTGGGAAAGGAWGCCAGACTGRTTATCARAACCTATTGGGGACTGC
CTACTTCCTAACGTGACTCTCTGTCCGATTGAAAGACCCTTTCCTWCGGTCTGACYAATAGTYTTGGATAACCCCTGACG
M K D C T E R Q A N F L G K X A R L X I X T Y W G L> 4780 4760 4770 4750 vif 61-90 (104) ATACCGGTGAGAGAGTGGCASCTCGGCCAWGGCGTCAGCATTGAGTGGAGGAYAAGGGGAAAGGGCTGAGGATAGCGGC
TATGGCCACTCTCTCTCACCGTSGAGCCGGTWCCGCAGTCGTAACTCACCTCTTTTCCCTTTTCCCGACTCCTATCGCCG
H T G E R D W X L G X G V S I E W R X R E R A E D S G>

FIGURE 15 (Cont)

SUBSTITUTE SHEET (RULE 26)

A5 join A6

4850 vpu 46-75 (135) **A6** join NESEGDXEELSXXVDMGNYDL **A7** 4950 4960 4920 4930 4940 env 510-539 (170) 4890 GGGACCCGATAGGCYGGRGRGAATCGAAGAGGAGGAGGCGGAGAGCRAGRCAGAGRCAGAAGCGTCAGGCTCGTGARTGGQA CCCTGGGCTATCCGRCCYCYCTTAGCTTCTCCTTCCGCCTCTCGYTCYGTCTCYGTCTTCGCAGTCCGAGCACTYACCGT P D R X X X I E E E G G E X X R X R S V R L 5030 5010 5020 4980 nef 151-180 (189) GWGAGGTCGAGGAARYCAATRAGGGAGAGAATAACTGTCTGCTCCACCCTATSRGTCWACATGGCATGGAAGACGAAGAS CWCTCCAGCTCCTTYRGTTAYTCCCTCTCTTATTGACAGACGAGGTGGGATASYCAGWTGTACCGTACCTTCTGCTTCTS V E E X N X G E N N C L L H P X X X H G M E D E X> 5100 5050 5060 5070 pol 961-990 (98) AGAGAGGTQAATAGCGATATCAAAGTGGTCCCCAGAAGGAAAGCCAAAATCATTAGGGATTACGGAAAGCAAATGGCTGG TCTCTCCAGTTATCGCTATAGTTTCACCAGGGGTCTTCCTTTCGGTTTTAGTAATCCCTAATGCCTTTCGTTTACCGACC R E V N S D I K V V P R R K A K I I R D Y G K Q M A G> 5160 pol 16-45 (35) 5130 5150 CGMTGACTGTGTGGCCRGGTTCYCTTCCGAGCAAACARGGGCTAACTCCYCTRCAAGCAGAAAGCTGGGAGACGGAGGGGG GCKACTGACACCGGYCGAAGRGAAGGCTCGTTTGTYCCCGATTGAGGRGAYGTTCGTCTTTCGACCCTCTGCCTCCGC X D C V A X F X S E Q T X A N S X X S R K L G D G G> 5220 5230 5240 5250 5210 gag 390-420 (27) GAGCCGASAGACAGGGAACAAGCTCCAGGTGTTTCAATTGCGGCAAAGAGGGACACHTTGCCARAAACTGTAGGGCCCCT CTCGGCTSTCTGTCCCTTCTTCGAGGTCCACAAAGTTAACGCCGTTTCTCCCTGTGKAACGGTYTTTGACATCCCGGGA G A X R Q G T S S S C F N C G K E G H X A X N C R A P> 5310 5320 5330 5340 5290 5300 CGCAAGAAAGGTTGTTGGAAATGCGGAARGGAAGGCCATCAAATGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTCGG GCGTTCTTTCCAACAACCTTTACGCCTTYCCTTCCGGTAGTTTACTTTCTGACATGCTTTCCGTTCGGTTAAAGGAGCC R K K G C W K C G X E G H Q H K D C T E R Q A N F L G> 5440 5400 5410 5420 5430 gag 421-450 (29) 5390 CAAAATCTGGCCCTCCMRCAAAGGCAGACCCGGAAACTTTCYCCAAAGGAAMTGGCTCTGGTATATCAAAATCTTTATCA GTTTTAGACCGGGAGGKYGTTTCCGTCTGGGCCTTTGAAAGRGGTTTCGTTKACCGAGACCATATAGTTTTAGAAATAGT
K I W P S X K G R P G N F X Q S X W L W Y I K I F I> 5490 5480 5450 env 465-494 (167) TGATCGTCGGTGGACTGRTTGGCCTCAGGATTRTCTTTGCCGTCCTGTCCATCRTTAACGGAGCCGYGAGCCRAGACCTCACTAGCAGCCACCTGACYAACCGGAGTCCTAAYAGAAACGGCAGGACAGGTAGYAATTTCCTCGGCRCTCGGYTCTGGAGMIV V G G L X G L R I X F A V L S I X N G A X S X D L> 5570 5580 spacers 5540 5530 nef 31-60 (181) GATAAACATGGCGCTHTTACAAGCTCCAATACCSCTGCCAATAACSCTGACTGTGYCTGGCTGRAGGCTGCCCATGAC CTATTTGTACCGCGAKAATGTTCGAGGTTATGGSGACGGTTATTGSGACTGACACRCACCGACYTCCG4CGACG4TACTG D K H G A X T S S N T X A N N X D C X W L X A A 5660 5670 - 5630 5620 vpu 1-30 (132) ACCCCTGGAGATCATCGCTATCGTCGCCYTTATCGTCGCCCTCATCMTAGCCATTGTGGTCTGGACAATCGYCTWCATTG TGGGGACCTCTAGTAGCGATAGCAGCGGRAATAGCAGCGGGAGTAGKATCGGTAACACCAGACCTGTTAGCRGAWGTAAC LEIIAIVAXIVALIXAIVVWTIXXI> 5720 pol 136-165 (43) 5710 5700 5690 **A7** AGTA GEGGAAATMTGCTCACCCAAMTCGGAYGCACACTGAATTTCCCTATCTCCCCCATTGASACAGTGCCTTGGAAA
TCATA AGAGCTTTAKACGAGTGGGTTKAGCCTRCGTGTGACTTAAAGGGATAGAGGGGGTAACTSTGTCACGGACACTTT ioin N X L T Q X G X T L N F P I S P I X T V P V K>

FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

**B**1

### 69/216

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env 255-284 (153)
         5770
                         spacers
                                              5800
                                                          5810
  CTGAAACCCGGAATGGATGGCCCCCCCAYCTTTAGGCCTGGCGGAGGCRATATSARAGACAATTGGAGAAGCGAACTGTA
  GACTTTGGGCCTTACCTACCGCGGCGGTRGAAATCCGGACCGCCTCCGYTATASTYTCTGTTAACCTCTTCGCTTGACAT
   L X P G N D G A A X F R P G G G X X X D N W R S E L Y>
                                                                                             5920
                                                          5890
                                                                     5900
                     5860
                                 5870
                                             5880
         5850
  TAAGTATAAGGTCGTGRAGATTRAGCCTCTGGGART(ACATGGATTCCCGAATGGGAGTTCGTCAACACACCCCCACTGG
 ATTCATATTCCAGCACYTCTANYTCGGAGACCCTYACTGTACCTAAGGGCTTACCCTCAAGCAGTTGTGTGGGGGTGACC
K Y K V V X I X P L G X T W I P E W E F V N T P P L>
                                                                                 5990
                                                                                             6000
                                                         5970
                                                                     5980
                                 5950
                                             5960
     pol 556-585 (71)
 TCAAGCTATGGTATCAGCTGGAGAAAGASCCTATCGYTGGCGYTGACCTCAGGATCTCAACAYGATGCTGAATAYTGTA
 AGTICGATACCATAGTCGACCTCTTTCTSGGATAGCRACCGCRACTCGGACTCCTAGAGTTGTRCTACGACTTATRACAT V K L W Y Q L E K X P I X G X E P Q D L N X M L N X V>
                                                         6050
                                                                     6060
                                                                                6070
                                             6040
                   gag 181-210 (13)
 GGAGGCCATCAGGCCGCTATCCAAATGCTGAAAGASACAATCAATGAGGAAGCCGCTGTCCTGTTTCTGGATGGCATTRA
 CCTCCGGTAGTCCGGCGATACGTTTACGACTTTCTSTGTTAGTTACTCCTTCGGCGACAGACAAAGACCTACCGTAAYT
G G H Q A A M Q M L K X T I N E E A A V L F L D G I X>
                               pol 706-735 (81)
                                                                                            6160
        6090
 CAAAGCTCAAGAGGAACATGAGARGTATCACTCCAACTGGAGGACAATGGCCARCGAMTTTAATCTCMTGAAGCATMTCG
 GTTTCGAGTTCTCCTTCTACTCTYCATAGTGAGGTTGACCTCCTGTTACCGGTYGCTKAAATTAGACKACTTCGTAKAGC
KAQEEHEXYHSNWRTMAXXFNLXKHX>
                                             gag 31-60 (3)
                                                                    6220
                    6180
                                6190
        6170
 TCTGGGCCTCTAGGGAGCTGGAGAGTTCGCTCTGAATCCCRGCCTGCTGGAGACAKCCGAAGGCTGTMAGCAAATTGCT
AGACCCGGAGATCCCTCGACCTCTCTAAGCGAGACTTAGGGYCGGACGACCTCTGTMGGCTTCCGACAKTCGTTTAACGA
    WASRELERFALNPXLLETXEGCXQI<sup>|</sup>A>
                                6270
                                            6280
                                                    env 215-244 (151)
        6250
 GAGGAAGAGATTATCATTACCTCCGAGAATYTCACARACAATGYCAAAACCATTATCGTCCAMCTCAACRAAAGCGTCGW
 CTCCTTCTCTAATAGTAATCCAGGCTCTTARAGTGTYTGTTACRGTTTTGGTAATAGCAGGTKGAGTTGYTTTCGCAGCW
  EEEIIIRSENXTXNXKTIIVXLNXS
                                                                                           6400
                                                        6370
                                                                    gag 1-30 (1)
                    6340
                                6350
                                            6360
        6330
GATTAAdATGGGCGCTAGGGCTAGTGTCCTCAGMGGCGGCRAGCTGGACGCCTGGGAAAAGATTAGGCTCAGGCCTGGCG
CTAATTCTACCCGCGATCCCGATCACAGGAGTCKCCGCCGYTCGACCTGCGGACCCTTTTCTAATCCGAGTCCGGACCGC
INHGARASVLXGGXLDAWEXIRLRPG>
                                                                   nef 91-120 (185)
                                                        6450
                                            6440
                               6430
                   6420
GAAAGAAAAGTATAGGCTCAAGGAGAAGGGGGGGCCTGGASGGACTGRTTTACTCCMAAAAGAGGCAAGASATTCTGGAT
CTTTCTTTTTCATATCCGAGTTCCTCTCCCTCCGGACCTSCCTGACYAAATGAGGKTTTCTCCGTTCTSTAAGACCTA
G K K K Y R L K E K G G L X G L X Y S X K R Q X I L D>
                                            6520
                                                        6530
                                                                   6540
                   6500
                               6510
       6490
CTGTGGGTGTATMACACACAGGGATTCAGTAGATGATGATGATCCTCGGCWTGGTGATKATCTGTAGCGCCAGCGA
GACACCCACATAKTGTGTGTCCCTAAGTGATGATCCCCTTGGWACTAGGAGCCGWACCACTAMTAGACATCGCGGTCGCT
                                                                                                   join
                                 TRWGTXILGXVXICSASX>
                                                                                                    B<sub>2</sub>
 LWVYXTQGF
                                                                   6620
                                                       6610
                               6590
                                           6600
    env 16-45 (138)
SAATCTGTGGGTGACAGTGTATTACGGAGTGCCTGTGTGGAGGAGACWGCTCCTGTCCGGCATTGTGCAACAGCAAARTA
STTAGACACCCACTGTCACATAATGCCTCACGGACACACCTCCTCTGWCGAGGACAGGCCGTAACACGTTGTCGTTIYAT
N L W V T V Y Y G V P V W R R X L L S G I V Q Q Q X>
                env 330-359 (158)
                                           6680
ACCTCCTGAGGGCTATCGAAGCCCAACAGCATCTGCTCCAGCTCACCGTCTGGGTCAGGCATTTCCCCAGGCCTTGGCTC
TGGAGGACTCCCGATAGCTTCGGGTTGTCGTAGACGAGGTCGAGTGGCAGACCGAGCCAGTCCGTAAAGGGGTCCGGAACCGAGN L L R A I E A Q Q H L L Q L T V W V R H F P R P W L>
```

FIGURE 15 (Cont)

vpr 31-60 (114)	6750	6760	6770	6780	6790	6800
CACRECCTGGGACAGYACATCTAT	GAGACATACO	GAGACACATG	GKMGGGAGTG	GAAGCCCTCAI	MAGCCC TCAT	CAMACC
CTCVVGG&CCCTGTCRTGTAGATA	CTCTGTATGC	CTCTGTGTAC	CMKCCCTCAC	TTCGGGAQT:	KTCGGG AGTA	GTKTGG
HXLGQXIY	E T Y	GDTW	X G V	E A L	XALI	X P>
6810 vif 151-18	0 (110)	6840	6850	6860	6870	6880
CAAAAAGATTARGCCTCCCCTCCC	. ,	A ACCTYC ACCC	AAGACARATGO	AATRAGCCT	TAYAGAYAT	ATAGCG
CTTTTCTAATYCGGAGGGGAGGG	PAGGCACTTT	TTCGAGTGGC	TICTGTYTACO	TTAYTCGGA(	<b>СТТТТСТ</b> ВТЈА	TATCGC Y S>
6890 6900	pol 901-9	30 (94)	6930	6940	6950	6960
CTGGCGAAAGGATTRTCGATATCAT	TTGCAWCCGA	CATTCAGACT.	AAGGAACTGC <i>A</i>	AAASCAAATO	MYAAAGATT	CAGAAT
GACCGCTTTCCTAAYAGCTATAGTA	ACGTWGGCT	GTAAGTCTGA'	TTCCTTGACGT	TTTSGTTTAG	SKRTTTCTAA	GTCTTA
6970 6980	6990	pol 886-9	15 (93)	7020	7030	7040
TTGCTGTGTTTATCCATAACTTTA	AGAGGAAGG	GAGGCATTGG	CGGCTACTCCG	CCGGAGAGAG	AATCRTTGAG	TATTAT
AACCGACACAAATAGGTATTGAAAT F A V F I H N F	TCTCCTTCCC	CTCCGTAACC	CCGATGAGGC	GGCCTCTCTC	TTAGYAACT	I I>
7050 7060	7070	•	gag 256-2		7110	7120
CGCCASCGATATCRTTCCCGTGGGC	GAWATCTATA	LAGAGATGGAT	rCATTCTGGGA	СТСААСАААА	TCGTGAGAAT	CTATY
GCGGTSGCTATACYAAGGGCACCCG	ርጥሡጥ ልር እጥ እግ	PTCTCTACCTA	<b>GTAAGACCCT</b>	GAGTTGTTTT	AGCACTCTTA	CATAR I Y>
AXDIXPVG	хіч	KKWI		LNK	1 0 10 10	
7130 7140	7150.	7160	•	nv 495-52		7200
MACCESTCAGEATTCTGGATATCAG	AGTGAGACAG	GGATACTCCC	CCCTCAGCTT	CAGACACTG	MYGCCCGCTC	CCAGA
KTGGGCAGTCGTAAGACCTATAGTC	TCACTCTGTC V R Q	CCTATGAGGG G Y S	EGGGAGTCGAA P L S F	Q T L	X P A	P R>
7210 7220	7230	7240	7250	7260	7270	7280
GGCCCTGACAGACAGACAGCACTACTACTACTACTACTACTACTACTACTACTACTACT	アイトアイトウィイ	GTCSGTCCTG	GTAGTCATAGO	GTAARGGCT	I C I C G C A C A C	YCTCA RGAGT % Q>
tat 61-90 (122)	7310	7320	7330	7340	7350	7360
GMCAAGGGGAGRCAATCCCACAGRCG CKGTTCCCCTCYGTTAGGGTGTCYGG X R G X N P T X	TO A VITCOTION	<u></u>	REFACCTCACC	AGC TCAGGT/	CTTATTCCT	IGACI IL
XRGXNPTX	PXE	2 1 1 1	5 0 1			_
⁷³⁷⁰ pol 856-88		7400	•	7420 1	7430	7440
AAAAGATTATCCGACAGGTCAGGGAN	CAGGCTGAG	CACCTGAAAA	CCGCTGTGCAA	ATGGCTGCCA	TGCAGATGCT	CAAG CTTC
TTTTCTAATAGCCTGTCCAGTCCCTK K K I I G Q V R X	(GTCCGACTC)	GTGGACTTTT(	GGCGACACGTT r A V Q	M A A	M Q M	L K>
KKIIGOVKX	Ų ,, Į		•			
, , , , ,	ag 196-22		•	7500	7510 i	7520
GAWACCATTAACGAAGAGGCTGCCGA C1WTGGTAATTGCTTCTCCGACGGCT X T I N E E A A E	CACCCTGTC	OCOTACOTHA OCOCATOCAY OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOCATOCA OCOC	OPPORTACY CAGGARAGA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CARACA CAR	ACCCRTTSCC TGGGYAASGG P X X	GGAGAGTGGC	SMGAT CKCTA X- I>
7530 7540		ool 181-21		*	7590 *	7600
TTGTAMAGAAATGGAAVAAGAAGGCA AACATKTCTTTACCTTBTTCTTCCGT C X E M E X E G	ጣጣጥ እር ልብርጥን	/CTAACCGGG/	TGAGAATCCCT ACTCTTAGGGA E N P	TATTGTGTGG	GINGAMMEGE	e in the
7610 7620	7630	7640	ool 871-90	0 (92)	7670	7680
AAGTGAGAGASCAAGCCGAACACCTC TTCACTCTCTSGTTCGGCTTGTGGAG	ママンファンマンマア	~ AGGTCTACCC	TC AGAAGTAA	GTGT TAAAGT	TITCCI I ICC	.000

REGURE 15 (Cont)

B3 join

**B4** 

#### 71/216

```
7760
                     7700
                                 7710
                                                                               7750
         7690
                                            pol 211-240 (48)
  atcggacgqaaaaagaagatagcacaaagtggaggaaactggtagactttagggagctcaacaaacgtacacaggattt
  TAGCCTCCCTTTTTCTTTCTATCGTGTTTCACCTCCTTTGACCATCTGAAATCCCTCGAGTTGTTTGCATGTGTCCTAAA I G G K K K D S \tau K W R K L V D F R E L N K R \tau Q D F>
                                                                                           7840
                                                                               7830
                                 7790
                                            7800
                                                      env 540-569 (172)
 CTGGGAGGTCCAGCTCGGCTTTTYGGCTCTGGCTTGGGATGACCTCAGGAGCCTGTGTCTGTTCAGCTATCACAGACTGA
GACCCTCCAGGTCGAGCCCGAAAARCCGAGACCGAACCCTACTGGACTCCTCGGACACAGACAAGTCGATACTGTCTGACT
W E V Q L G F X A L A W D D L R S IL C L F S Y H R L>
                                                        7890
                                                                  vpr 76-96 (117)
                                7670
                                            7880
                    7860
        7850
 GAGACYTTATCCTCATCGYTGCCAGAAYCTGCCRACATAGCAGAATCGGCATCACTAGGCAACGTAGAGSTAGGAACGGC
 CTCTGRANTAGGAGTAGCRACGGTCTTHCACGGYTGTATCGTCTTAGCCGTAGTGATCCGTTGCATCTCSATCCTTGCCGR D X I L I X A R X C X H S R I G I T R Q R R X R N G>
                                                       7970
                                7950
                                            7960
                                                                 env 155-184 (147)
             spacers
 KCCTCCAGGTCGGCTGCCCCAAARTCWCCTTCGAMCCCATTCCCATTCACTATTGCGCTCCCGCTGGCTWCGCTATCCT
 HGGACGTCCAGCGACCGGGGTTTYAGWGGAAGCTKGGGTAAGGGTAAGTGATAACGCGAGGGCGACCGAWGCGATAGGA
  X S R S A A P R X X F X P I P I H Y C A P A G X A I L>
                                                                                          8080
                                           8040
                                                       8050
                    8020
                               8030
                                                                  vif 76-105 (105)
 CAACTGTAACRATAAGAMMTTCAATGGCGAAARGGATTGGCAWCTGGGACASGGAGTGTCCATCGAATGGAGAMMGAAAA
 GTTCACATTGYTATTCTKKAAGTTACCGCITTYCCTAACCGTWGACCCTGTSCCTCACAGGTAGCTTACCTCTKWCTTTT
K C N X K X F N G E X D W X L G X G V S I E W R X K>
                                                       8130
                                           8120
                                                                 gag 481-499 (33)
        8090
                    8100
XYSTQVDPXLADQP
                                                  SLYPPXASLKSLF>
                    spacers
                                                       8210
        8170
                                           8200
                                                                vif 121-150 (108)
GGAAACGATCCCTYATCCCA/GCCGCTAGAAGGGCTATCCTCGGCCAWAKAGTCAGSAGAAGGTGTGAGTATCMGKCCGG
CCTTTGCTAGGGARTAGGGTTCGGCGA/CCTTCCCGATAGGAGCCGGTWTMTCAGTCSTCTTCCACACTCATAGKCMGGCC
G N D P X S Q A A R R A I L G X X V X R R C E Y X X G>
                                           8280
                                                      8290
                   8260
                               8270
ACACANTAAGGTCGGCTCCCTGCANTACCTCGCACTQAGCCANCCCMMAACCGCTTGCWMCAAGTGTTACTGTAAGAAAT
TGTGTTATTCCAGCCGAGGGACGTTATGGAGCGTGAGTCGGTTGGGTKTTGGCGAACGWKGTTCACAATGACATTCTTTA
H N K V G S L Q Y L A L S Q P X T A C X K C Y C K K>
                                                      8370
                               8350
                                           8360
                                                                pol 976-995 (99)
    tat 16-45 (119)
GTTGCTWCCACTGTCAGSTCTGCTTCCTGAMGAAGGGACTGGGAATQAGGGATTACGGAAAGCAAATGGCTGGCGMTGAC
spacers
                                                      8450
                                                                pol 721-750 (82)
       8410
8540
                                                      8530
                              8510
                                          8520
CCCTATCGTCSCTAAGGAAATCGTCGCAWRTTGCGATAAGTGTAACGAATCGRCACTGGAACTGCTGGAGGAACTGAAAAM
GGGATAGCAGGGATTCCTTTAGCAGCGTWYAACGCTATTCACATTGCTTACCYGTGACCTTGACGACCTCCTTGACTTTK
P I V X K E I V A X C D K C N E W X L E L L E E L K>
                                                                                        8640
                                                                 8620
                                                                             8630
                                          8690
                                                      8610
                              8590
     vpr 16-45 (113)
AWGAAGCCGTGAGACACTTTCCCAGACCCTGGCTGCATGGCCTCGGTCAACAGATRTCATTAGCCTCTGGGATCAGTCC
TWCTTCGGCACTCTGTGAAAGGGTCTGGGACCGACGTACCGGAGCCCAGTTGTCCTAYAGTAATCGGAGACCCTAGTCAGG
X E A V R H F P R P W L H G L G Q H D X I S L W D Q S>
```

FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

env 106-144 (144) CTGAAACCCTGTGTGAAACTGACACCCCTGTGCGTCACCCTCAACTGTACCAATGCCAATCTGHGGAAGAGHTACTCCAC GACTTTGGGACACACTTTGACTGTGGGGAGACGCAGTGGGAGTTGACATGGTTACGGTTAGACKWCTTCTCKATGAGGTG L K P C V K L T P L C V T L N C T N A N L X K X Y S T> 8790 8800 8730 8740 8770 8780 vif 91-120 (106) CCAAGTGGACCCCGRTCTGGCTGACCAWCTGATTCACCTCCACTATTTCGATTGCTTTKCCGATAGCRCAATCCACCA GGTTCACCTGGGGCYAGACCGACTGGTWGACTAAGTGGAGGTGATAAAGCTAACGAAAMGGCTATCGYGTTAGGTAGGGT Q V D P X L A D X L I H L H Y F D C F X D S X I H P> 8870 8820 8830 nef 166-195 (190) 8860 8810 TSRUCCWACACGGAATGGAGGATGAGGAWAGGGAAGTGCTGAWATGGAAATTCGATAGCCRTCTGGCTCKCAGGCATATS ASYCGGWTGTGCCTTACCTCCTWTCCCTTCACGACTWTACCTTTAAGCTATCGGYAGACCGAGMGTCCGTATAS X X X H G M E D E X R E V L X W K F D S X L A X R H X> pol 151-180 (44) 8920 8900 8910 GCTTTTTGAWACCGTCCCCGTCAAGCTCAAGCTCGACGGACGGACCCAAAGTGAAACAGTGGCCCCTCAC CG CGATACCTWTGGCAGGGCAGTTCGAGTTCGGACCGTACCTGCCTTGAGTTCACTTTGTCACCTGCGGGGGTG

A S S P I X T V P V K L K P G M D C P K V K O W P I. PIXTVPVKLKPGMDCPKVKQWPL gag 436-465 (30) 9000 9010 8970 8980 8990 CGAAGAGAAAATCAAAGCCATTTGGCCTAGCMRCAAGGGAAGGCCTGGCAATTTCCYGCAGTCCARGCCTGAGCCTACCG CCTTCTCTTTTAGTTTCCGTAAACCGGATCGKYGTTCCCTTCCGGACCGTTAAACGRCGTCAGGTYCGGACTCGGATGGC
E E K I K A I W P S X K G R P G N F X Q S X P E P T> 9080 vif 31-60 (102) 9120 9050 9060 9070 9090 CACCCCAGCCGAGARCTTTRGATTCGGGATTAGCAAAAAGGCTAASGGATGGTTTTACAGACACCATTWCGAWAGCCRA A P P A E X F X F G I S K K A X G W F Y R H H X X S X> 9140 9150 9160 9170 9180 9190 9200 9130 CACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCGGATGATGACGGCTTGCCAAGGCGTCGGCGGACCCRGTCACAA CTCGCATTCCACTCGAGGCTCCAGGTGTAAGGGGAGCCCTACTACTGCCGAACGGTTCCGCAGCCGCCTGGGYCAGTGTT
H P K V S S E V H I P L G M N T A C Q G V G G P X H K> 9260 9280 gag 346-375 (24) 9230 9240 9250 AGCCAGGGTACTGGCAGAGGCTATGTCCCAGGYGAMCMACGCTAACATTCCTCCCATTGTGSCCAAAGAGATTGTGGCAW TCGGTCCCATGACCGTCTCCGATACAGGGTCCRCTKGKTGCGATTGTAAGGGAGGGTAACACGGGTTTCTCTAACACCGTW
ARVLAEAMSQXXXANIPPIVXKEIVA> 9330 9340 9290 pol 736-765 (83) 9320 RCTGTGACAAATGCCAGCTCAAGGGTGAGGCTATKCACGGACAGGTGRACTGTAGCCCQTCCGAGGGAWCAAGACAGRCT YGACACTGTTTACGGTCGAGTTCCCACTCCGATAMGTGCCTGTCCACYTGACATCGGGAAGCCTCCCTWGTTCTGTCYGA
X C D K C Q L K G E A X H G Q V X C S P S E G X R Q X> 9420 9440 9380 rev 31-60 (126) 9410 AGGARGAACAGACGTAGAAGGTGGCGTGMGAGGCAAAGGCAAATCCRCKCCATCTCCGAGWGGATTCTGGGACAGATRAG 9510 9470 9500 9460 gag 226-255 (16) GGAACCCAGAGGCTCCGACATTGCCGGTACCACAAGCACACTGCAAGAGCAAATCGSATGGATGACAARCAATCCCCC4R CCTICGGTCTCCGAGGCTGTAACGGCCATGGTGTCGTGTGACGTTCTCGTTTAGCSTACCTACTGTTYGTTAGGGGGA EPRCSDIAGTTSTLQEQIXWMTXNPP> 9550 9560 9530 9540 pol 841-870 (90) RCATTMAGCAAGAGTTTGGCATTCCCTATAACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTCAAGAAA YGTAAKTCGTTCTCAAACCGTAAGGGATATTGGGAGTCAGGGTCCCGCAGCACCTTTCGTACTTGTTTCTCGAGTTCTTT X I X Q E F G I P Y N P Q S Q G V V E S M N K E L K K>

FIGURE 15 (Cont)

SUBSTITUTE SHEET (RULE 26)

B4 join B5

**B**5

**B6** 

# 73/216

```
nef 106-135 (186)
                                                                                  9670
                                                                                               9680
                      9620
                                  9630
          9610
  ATCATTGGQAGACAGGAGATCCTCGATCTCTGGGTCTACMATACCCAAGGCTWTTTCCCTGACTGGCASAATTACACACC
  TAGTAACCGTCTGTCCTCTAGGAGCTAGAGACCCAGATGKTATGGGTTCCGAWAAAGGGACTGACCGTSTTAATGTGTGG
I I G R Q E I L D L W V Y X T Q G X F P D W X N Y T P>
                                                                                  9750
                                              9720
                                  9710
                                                         rev 46-75 (127)
          9690
  CGGACCCGGARYCAGATA(GCGACCAGACAGACAGACAGACTCRTKCTATTAGCGAAWGGATTCTCAGCAMCTKCCGCCTGGGCCTYRGTCTATCGGAGGTCGTKGAMGG
                                                                                                       join
                          PSRXRQRQIXXISEXILSXX>
                                                                   gag 301-330 (21)
                                                                                               9840
                     9780
                                  9790
                                              9800
                                                          9810
         9770
  TCGGCAGAYCCGCTGAGCCTGTGCCTCTGCAACTGTWTAAGACACTGAGAGCCGAACAGGCTWCCCAAGASGTCAAGAAT
  AGCCGTCTRGGCGACTCGGACACGGAGACGTTGACAWATTCTGTGACTCTCGGCTTGTCCGAWGGGTTCTSCAGTTCTTA
L G R X A E P V P L Q L X K T L R A E Q A X Q X V K N>
                                                                     9900
         9850
                     9860
                                 9870
                                             9880
                                                          9890
  TGGATGACCGASACACTGCTCGTGCAAAACGCTAACCCTGACTGTGAGARAGTGTATCTGKCTTGGGTCCCCGCTCATAA
 ACCTACTGGCTSTGTGACGACCACGTTTTGCGATTGGGACTGACACTCTTTCACATAGACMGAACCCAGGGGGGAGTATT W M T X T L L V Q N A N P D C E X V Y L X W V P A H K>
                                                                                 9990
                                 9950
                                             9960
                                                         9970
                                                                     9980
      pol 676-705 (79)
 AGGCATTGGCGGAAACGAACAGGTGGACAAACTGGTCAKCKCTGGCATTAGGAAAACAGACCCTAACCCTCAGGAARTCS
 TCCGTAACCGCCTTTGCTTGTCCACCTGTTTGACCAGTMGMGACCGTAATCCTTTTGTCTGGGATTGGGAGTCCTTYAGS
GIGGNEQVDKLVXXGIRKTDPNPQEX>
                                           10040
                                                        10050
                  env 76-105 (142)
 WTCTGGAAAACGTCACCGAGAACTTTAACATGTGGAAAAACRATATGGTGGASCAAATGCAWGAGGCTGGCTWTGCCATT WAGACCTTTTGCAGTGGCTCTTGAAATTGTACACCTTTTTGYTATACCACCTSGTTTACGTWCTCCGACCGAWACGGTAA X L E N V T E N F N M W K N X M V X Q M X E A G X A I>
                             env 170-199 (148) 10130
                   10100
                                                                   10140
       10090
 CTGAAATGCAATRACAAAAMSTTCAACGGAACTGGACCCTGTAHGAATGTGTCCASCGTCCAGTGTACCCATGGCWAGA
 GACTTTACGTTAYTGTTTTKSAAGTTGCCTTGACCTGGGACATKCTTACACAGGTSGCAGGTCACATGGGTACCGGWTCT
L K C N X K X F N G T G P C X N V S X V Q C T H G X E>
                                         env 600-629 (176) 10220
                               10190
       10170
GCTCAAGAWTAGCGCTRTCTCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGRGKGGACCGATAGGRTTATCGAAGTGG
CGAGTTCTWATCGCGAYAGAGGGACGAGTTGCGATGGCGATAGCGACACCGACYCHCCTGGCTATCCYAATAGCTTCACC
   L K X S A X S L L N A T A I A V A X X T D R X I E V>
                                                                               10310
                              10270
                                           10280
                  10260
      10250
                                                      vif 46-75 (103)
YTCACTCCCRGCATCCCAAACTCTCCAGCGAAGTGCATATCCCTCTGGGAGASGCTAGGCTCRTCATTARGACATACTGG
RAGTOAGGGYCGTAGGGTTTCACAGGTCGCTTCACGTATAGGGAGACCCTCTSCGATCCGAGYAGTAATYCTGTATGACCXXQSXHPKVSSEVHIPLGXARLXIXTYW>
                                           10360
                                                      10370
               spacers
      10330
                                                                   nef 1-30 (179)
GGCCTCCASACAGGGGCTGCTATGGGCGGTAAATGGTCCAAGWCCTCCCYCGTCGGATGGCCCGMAGTGAGAGAGAGAAAT
CCGGAGGTSTGTCCCGCGATTACCCGCCATTTACCAGGTTCWCGAGGGGGCAGCCTACCGGGCKTCACTCTCTCTTA

G L X T G A A M G G K W S K X S X V G W P X V R E R I>
                                                                                          10480
                  10420
                              10430
                                          10440
                                                      10450
                                                               pol 496-525 (67)
      10410
CAGACRGRCASCCCCTGCCGCTGAGGGAGTGCTCAAGACCGGCAAGTACKCTAGGAWGAGGRGTGCCCATACCAATGACG
GTCTGYCYGTSGGGACGCGACTCCCTCAGGGTTCTGGCCGTTCATGMGATCCTWCTCCYCACGGGTATGGTTACTGC
R X X P A A E G V L K T G K Y X R X R X A H T N D>
                                                                              10550
                                                                                          10560 B6
                                                                  10540
                                          10520
                                                      10530
                 10500
                              10510
TCARGCAACTGACAGMGGYTGTGCAAAAGATTGCCACAGATTTAGGTTGGGAGGSTCTGAAATACTKGKGGAATCTGCTC
AGTYCGTTGACTGTCKCCRACACGTTTTCTAACGGTGTCTCAGATGGACCCTCCSAGACTTTATGAMCMCCTTAGACGAG
B7
V X Q L T X X V Q K I A T E S S W E X L K Y X X N L L>
```

FIGURE 15 (Cont)

SUBSTITUTE SHEET (RULE 26)

env 585-61		10590	10600	10610	10620	10630	10640					
CWGTACTGGGGCCWGGAACTGAAAAWCTCCGCCRTCAGGCTCCTGAATGCCACAGCCATTSWGCTGCCTGAGAAAGAWAG GWCATGACCCCGGWCCTTGACTTTTWGAGGCGGYAGTCGGAGGACTTACGGTGTCGGTAASWCGACGGACTCTTTCTWTC												
	COURSE A COURT	የጥሠር አርርርርር	V ACTCGGAGG	<b>ACTTACGGT</b> (	STCGGTAASWC	GACGGACTUT	TICIMIC					
X Y W G	XELK	хѕл	X S,L	LNA	. A.I Y	LFL	K X 5-					
10650	pel 391-4		10680	10690 *	10700	10710	10720					
CTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCATCCCAGATTACSCCGGAAGAGCCCATTGAGG GACCTGGCAGTTGCTATAGGTTTTCGAGCACCCTTTCGAGTTGACCCGTAGGGTCTAAATGSGGCCTTCTCGGTAACTCC												
GACCTGGCAGTTGG W T V. N	TATAGGTTTT D I Q K	CGAGCACCC L V G	K L N	W A S	Q I Y X	G R A	I E>					
10730		nv 345-3		10770	10780	10790	10800					
CTCAGCAACACWTGCTGCAACTGACAGTGTGGGGGCATTAAGCAACTGCAAGCCAGAGTGCTCGCCRTTGAGAGATACCTC GAGTCGTTGTCWACGACGTTGACTGTCACACCCCGTAATTCGTTGACGTTCGGTCTCACGAGCGGYAACTCTCTTATGAG												
CAGTCGTTGTGWAC	GACGTTGACT L Q L	T V W	G I K Q	L Q A	R V L	X E R	Y L>					
10810	10820	10830	pol 631-6	•	10860	10870	10880					
CCCCTCCAGGATAG	CGGATYGGAA	GTGAATATC	STCACCGATAC	CCAATACGC	TCTAGGCATC	TTCWGGCTCA	GCCTGA					
GCCCTCCAGGATAGCGGATYGGAAGTGAATATCGTCACCGATAGCCATACGCTCTAGGCATCATTCWGGCTCAGCCTGA CGGGAGGTCCTATCGCCTARCCTTCACTTATAGCAGTGGCTATCGGTTATGCGAGATCCGTAGTAAGWCCGAGTCGGACT A L Q D S G X E V N I V T D S Q Y A L G I I X A Q P D>												
10890	10900	10910	10920	env 420-4	49 (164)	10950	10960					
CARAAGGGAAAGGG	AAATCTCCAA	CTATACCART	CWGATTTACE	AGATCCTCA	CCGAATCTCAA	AATCAACAGG	ATAGGA					
GTYTICGCTTTCCC		へりかりがつだかりと	CWCTAAATGY	TCTAGGAGT	SCCTIAGAGIT	TINGTIGIC	INICCI					
10970	10980	10990	11000		env 285-3		11040					
ATGAGMAAGASCTC	andecasees	* ************************************	CDODAGAGE	* CTCSAAAGGC	BAAAAGCGTGC	CGTCGGCMTT	CGCGCT					
TACTCKTTCTSGAG	GACGAGGGTC	こかがひつつひかかて	CTCTTCCCAG	CACSTITUU	TTTTTCGCACG	GCAGCCGKAA V G X	ccocon					
11050	11060	11070	11080	11090	pol 91-12	0 (40)	11120					
ATGWTTYTCGGATT	CCTCGGCGCTG	cdaaaccca	AAATGATCGG.	AGGCATTGGA	GGCTTTATCA	AAGTCAGGCAG	STATGA					
		COTTTCCCT	ጥጥጥ ልርጥ ልርርር '	TCCGTAACCI	CCGAAATAGT	TICACICCOIC	WINCI					
M X X G F	L G A	A'K P	K M I G	GIG	G P 1	K V K Q	. 5-					
11130	11140	11150	11160	11170	11180	11190	11200					
CCAAATCHTTATCGA GGTTTAGKAATAGCT Q I X I I												
, I, A I U						11270	11280					
env 555-584	(,,,,,,	11230	11240	11250	11260	•	•					
YTGTGGAACTGCTCG RACACCTTGACGAGG	GCCRTAGCTC	CCTGARAGG	CCTCCRGAGA( CGAGGYCTCT(	CCTACACTGA CCTGTGACT	TACGGACCUA	JIIICAC I ANC	10011					
X V E L L	C X S S	L X G	L X R	G T L	V W A M	K V X	E E>					
11290 g	gag 151-18	0 (11)	11320	11330	11340	*	11360 T					
AAGGSATTCARTCCC TTCCSTAAGTYAGGC	GAAGTGATTC CTTCACTAAG E V I	CCTACAAAW	GCGAGACAGC	CTCCCTCGG	TOTORGETAL	.6116161366	GCTAA					
кхгхр	E V 1	P 19 F .					1					
11370		nef 46-75		11410	11420	• 1	11440					
CAATSCCGATTGCGYGTGCTGRAAGCCCAGGAAGAGGAAGRAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCCK GTTASGGCTAAGGCRCACCGACYTTCGGGTCCTTCTCCTTCYTCACCCTAAAGGACACTCTGGGGTTCACGGATCTCGGM												
GTTASGGCTAACGCF N X D C X	CACCGACYTT	CGGGTCCTTC	E E X V	G F P	V R P	Q V P R	A>					
	าง 630-651		•	11490	spacer	- 1	11520					
GGAGGGCTATCCTCM CCTCCCGATAGGAGK X R A I L	CTODOA ACCOTS	CTCCTAATC	GTTCCGRAAC	TCTCTCGGG	<b>NGGATIC GGCGC</b>	IC I I MCCCC I WI	CCIM					
V K W T P	~ · · ·	,			L	•						

FIGURE 15 (Cont)

SUBSTITUTE SHEET (RULE 26)

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11600
                                                                 11590
                                                       11580
                                             11570
                        gag 211-240 (15)
               13,540
     11530
CACCTGTGCACGCTGGCCCTRTCSCTCCCGGCCAAATSAGAGAGCCCAGGGGAAGCGATATCGCTGGCACAACCCTCAG
GTGGGACACGTGCGACCGGGAYAGSGAGGGCCGGTTTASTCTCTCGGGTCCCCTTCGCTATAGCGACCGTGTTGGGAGTC
HPVHAGPXXPGQXREPRGSDIAGTTLR>
                                                       11660
                         11630
                                   nef 76-105 (184)
               11620
GCCCATGACATATAAGGSCGCTRTIGACCTCAGCYTGTTTCTGAAAGAGAAAGGCGGACTGGAWGGCCTCRTCTATAGCM
CGGGTACTGTATATTCCSGCGAYAACTGGAGTCGRACAAAGACTTTCTCTTTCCGCCTCACCTWCCGGAGYAGATATCGK
  PMTYKXAXDLS LFLKEKGGLXGLXYS>
                                                                            11760
                                                                 11750
                                              vpr 1-30 (112)
                                   11720
                         11710
AGAAAGCTGCTATGGAACAGGCTCCCGAAGACCAARGCYCTCAGAGAGAGCCTTACAATGAGTGGRCCCTGGAGCTCCTG
    spacers
TCTT CGACGATACCTTGTCCGAGGGCTTCTGGTTYCGRGAGTCTCTCTCGGAATGTTACTCACCYGGGACCTCGAGGAC
X K A A M E Q A P E D Q X X Q R E P Y N E W X L E L L>
                                                       pol 481-510 (66)
                                             11810
                         11790 11800
GAAGAGCTCAAGMAMGAGGCTCAAGRCCAATGGACCTWCCAAATCTWTCAGGAACCCTTTAAGAATCTGAAAACCGGAAA
CTTCTCGAGTTCKTKCTCCGAGTTCYGGTTACCTGGAWGGTTTAGAWAGTCCTTGGGAAATCTTTAGACTTTTGGCCTTT
E E L K X E A Q X Q W T X Q I X Q E P F K N L K T G K>
     11770
                                                                 11910
                                                       11900
                                   11880
                                              11890
                         11870
               11860
GTATKCCAGAAWGAGARGCGCTCACACAAACTGGATGACAGAWACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGW
     11850
CATAMGGTCTTWCTCTYCGCGAGTGTGTTTGACCTACTGTCTWTGGGAGGACCAGGTCTTACGGTTAGGGCTAACGTTCW
Y X R X R X A H T N W M T X T L L V Q N A N P D C K>
                                                                 11990
                                                       11980
                                              11970
                                    11960
                         11950
  gag 316-345 (22)
CCATCCTCARGGCTCTGGGAMCCGGAGCCWCACTGGAAGAGCCTGAGGTCATCCCTATGTTCWCAGCCCTCAGCGAAGGC
GGTAGGAGTYCCGAGACCCTKGGCCTCGGWGTGACCTTCTCGGACTCCAGTAGGGATACAAGWGTCGGGAGTCGCTTCCG

X I L X A L G X G A X L E E P E V I P M F X A L S E G>
                                                       12060
                                              12050
                                    12040
               gag 166-195 (12)
      12010
GCTACCCCCAAGACCTGAATAYGATGCTCAACAYCGTCGGCGGACACCAATCCACCCTCCAGGAACAGATTGSCTGGAT
CGATGGGGGGTTCTGGACTTATRCTACGAGTTGTRGCAGCCGCCTGTGGTTAGGTGGGAGGTCCTTGTCTAACSGACCTA

A T P Q D L N X M L N X V G G H Q S T L Q E Q I X W M>
                                                                 12150
                                                        12140
                         gag 241-270 (17)
                                             12130
                                                                                    C1
                12100
12090
                                                                                   join
                                                                                    C2
  TXNPPXPVGXIYKRWIILGLTR
                                                                  12230
                                                        12220
                                   pol 241-270 (50)
                          12190
                12180
      12170
CCGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACRAARRCCAA
GGCCGGAGTTCTTTTCTTTTCGCAGTGGCAGGACCTACACCCTCTGCGAATGAAGTCGCAGGGGGAGCTGYTTYYGGTT
AGLKKKSVTVLDVGDAYF5VPLDXX<sup>1</sup>Q>
                                                                  12310
                                             pol 541-570 (70)
                                    12280
                          12270
                12260
\tt ARGGAAACCTGGGAGRCTTGGTGGAYGGAMTACTGGCAGGCTACCTGGATTCCTGAGTGGGAGTTTGTGAATACCCCTCC
 TYCCTTTGGACCCTCYGAACCACCTRCCTKATGACCGTCCGATGGACCTAAGGACTCACCCTCAAACACTTATGGGGAGG
 X E T W E X W W X X Y W Q A T W I P E W E F V N T P P>
                                                                            12400
                                                       nef 121-150 (187)
                                              12370
                                    12360
                          12350
                12340
      12330
 CCTCGTCTTTCCCGATTGGCAWAACTATACCCCTGGCCCTGGCRYAAGGTATCCCCTCACCTTTGGATGGTGCTTTAAGC
 GGAGCACAAAGGGCTAACCGTWTTGATATGGGGACCGGGACCGYRTTCCATAGGGGAGTGGAAACCTACCACGAAATTCG
L V F P D W X N Y T P G P G X R Y P L T F G W C F K>
                                                       pol 571-600 (72)
                                              12450
                                    12440
                          12430
                12420
      12410
 TCGTGCCTGTGGACCCCQAAACTGTGGTACCAACTGGAAAAGGAMCCCATTGYCGGAGYCGAAACCTTTTACGTGGACGGA
 AGCACGGACACCTGGGTTTGACCACCATGGTTGACCCTTTTCCTKGGGTAACRGCCTCRGCTTTGGAAAATGCACCTGCCT
```

# FIGURE 15 (Cont)

				400	(4.0)						
12490	12560	12510	•	gag 136		12550	12560				
GCCGCCARCAGAG. CGGCGGTYGTCTC	AGACAAAGC1	CGGCCAAAA	SYCCAGGGA	AGATGGTGC	ATCAGSCTMTT	AGCCCCAGGA	ACCCTCAA TGGGAGTT				
A A X R	E T K L	G Q N	X Q G	Q M V	н о х х	S P R	T L N>				
12570	12580	12590	12600	12610	env 61-90	•	12640				
CGCTTGGGTCAAGGTCRTCGAAGAGAAAGSCTTTARCGAMACCGAAGTGCATAACGTCTGGGCTACCCATGCCTGTGTGC GCGAACCCAGTTCCAGYAGCTTCTCTTTCSGAAATYCTTKTGGCTTCACGTATTGCAGACCCGATGGGTACGGACACACG											
A W V K	V X E	E K X F	XXXT	E V H	N V W A	тна	C V>				
12650	12660	12670	12680	12690	12700	12710	12720				
CTACCGATCCCAAT GATGGCTAGGGTTA P T D P N	GGGGTTCTC	YAASWGGACC'	TCTTACACTG	<b>ፕሮ</b> ፕ₫ <b>₢</b> እ <b>₢</b> ፕፕ(	CCTAGTCKTTRA	<b>AGGAGCCGKA</b>	AACCCCT				
env 375-40	04 (161)	12750	12760	32770	12780	12790	12800				
TGCTCCGGCAAAMT	CATTTGCAC	ACCRMTGTG	CTTGGAACA	GCWCCTGGT(	CAACHAKCTO	GCCATAACA	AAGTGGG				
ACGAGGCCGTTTKA	CTAAACCTC1	PTCCYKACACO	GAACCTTGT	CGWGGACCAC	GTTGGKTMGAC	CGGTATTGT	TTCACCC				
12810 V	if 136-16	5 (109)	12840	12850	12860	12870	12880				
AAGCCTCCAGTATC TTCGGAGGTCATAG	TGGCTCTGAN	GGCTCTGATT	AMGCCTAAG	AAATCARAC	CCCCTCTGCCT	AGGGYTAAG	ACAATCA FGTTAGT				
TTCGGAGGTCATAG S L Q Y	ACCGAGACTR L A L X	CCGAGACTAA	X P K	K I X	P P L P	s x K	T I>				
12890	12900	env 230-2	54 (152)	12930	spac	ers	12960				
TTGTGCATCTGAAT	RAGTCCGTGG	WAATCAATTG	CACAAGGCCT	'ARCAATAAC	ACAAGGAMAGC	ccccccinici	GAAGWA C2				
AACACGTAGACTTA	YTCAGGCACC	WTTAGTTAAC	GTGTTCCGGA	TYGTTATTG	TOTAL COLLEGE	CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	erremi join				
12970	12980	•	gag 106-1		13020	13030	13040				
CAGAAWAAGTCCMAX GTCTTWTTCAGGKTT	CAGAAAACC	CAGCAAGCCG	CCCCCGATAC	AGGCARCTC	CAGCMAGGTCAG	CCAAAACTA CGGTTTTGAT	TCCCAT				
C X K S X	Q K T	Q Q A	A A D T	G X S	s x v	S Q N Y	P I>				
13050	13060	13070	13080	pol 826-	855 <b>(89</b> )	13110	13120				
TGTCTCCAACTTTAC	CTCCRCCRC	rgtgaaagcco	CTTGTTGGT	GGGCCRRTAT	CMAACAGGAG?	TTGGAATCC AACCTTAGG	CTTACA GAATGT				
V S N F T	s x x	V K A	A C W	WAXI	X Q E	PGI	P Y>				
13130	13140	13150	13160	13170	pol 586-61	5 (73)	13200				
ATCCCCAAAGCCAAA TAGGGGTTTCGGTTT	GTAAGATAC?	CCTACCGCG	CGGTYATCC	TTTGGTTTC	BACCCTTTCCGA	CCGATACACT	TGTCTG				
N P Q S Q	TFY	DGA	A X R	E T K	L G K A	G Y V	T D>				
13210	13220	13230	13240	13250	pol 766-79:	5 (85)	13280				
AGAGGCAGACAGAAA	RTCRTTAGG	GAATCTGGCA	GCTCGACTGT	ACCCATCTG	GÁAGGCAAART	CATTCTGGT	AGCCGT				
TCTCCGTCTGTCTTT R G R Q K	YAGYAATCO X X S	CTTAGACCGT G I W Q	CGAGCTGACA L D C	T H L	E G K X	I L V	A V>				
13290	13300	13310	13320	13330	13340	13350	13360				
• CCACGTCGCCTCCGG	CTACATTGAG	CCTGAGGTC	GCAATGAGCA	AGTGGATAA	GCTCGTGAKTK	CCGGAATCAG	BAAAGG				
GGTGCAGCGGAGGCC H V A S G	CATCTAACTC	CCACTCCACC	CGTTACTCGT	TCACCTATT	CGAGCACTMAM	GGCCTTAGTC	TTTCC				
							13440				
pol 691-720		•	- 1	•	*	,	,				
TGCTATTCCTCGACG	GAATCRATAA	GGCTCAGGAA	GAGCACGAZO	ፕሮአርርርሌ ትርፕርርር የተሞ	GGATTAGGCRA CCTAATCCGYT	RCCSCTCCCG YGGSGAGGGC	CTGCT GACGA				
ACGATAAGGAGCTGC V L F L D	CIAGIIAIT	λ Q E	E H E	V R E	RIRX	х х Р	A A> ·				

PIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

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13480
                                             13490
                         13470
     nef 16-45 (180)
  GAAGGCGTCGCCCTGYCTCCCRGGATCTGGATAAGKACGGAGCCMTCACCTCQACAAGCGGAACCCAACAGTCCCAGGG
  CTTCCGCAGCCGCACRGAGGGYCCTAGACCTATTCMTGCCTCGGKAGTGGAGGTGTTCGCCTTGGGTTGTCAGGGTCCC
E G V G A X S X D L D K X C A X T S T S G T Q Q S Q G>
                                                                          13600
                                            13570
                                                      13580
                                                                13590
                                   13560
      13530
               rev 91-120 (130)
 AACTGAAACTGGCGTCGGCMRCCCTCAGATTIYGGGAGAGTCCAGCGYTRTCCTCGGCYCCGGGTCCATCGTCATCTGGG
 TTGACTTTGACCGCAGCCGKYGGGAGTCTAAARCCCTCTCAGGTCGCCRAYAGGAGCCGRGGCCGAGGTAGCAGTAGACCC
T E T G V G X P Q I X G E S S X X L G X G S I V I W>
                                                                      spacers
                                            13650
                                                      13660
      13610
               13620
                       pol 526-555 (69)
 GTAAAACCCCTAAGTTTARGCTCCCCATTCAGARAGAGACATGGGAARCCTGGTGGAYGGASTATTGGCAAGCCGCTGCT
 13690
               13700
                         13710
                                 env 140-169 (146)
                                                     13740
 TACAGACTGATCARCTGTAACACAAGCGYTATCAHACAGGCTTGCCCTAAGRTTASCTTTGASCCTATCCCTATCCATTA
 ATGTCTGACTAGTYGACATTGTGTTCGCRATAGTKTGTCCGAACGGGATTCYAATSGAAACTSGGATAGGGATAGGTAAT
  Y R L I X C N T S X I X Q A C P K X X F X P I P I H Y>
                                                               13830
                         13790
                                  13800
                                           pol 376-405 (59)
 PSWMGYELHFDRWTVQPIXLPEK>
                                                     gag 331-360 (23)
                         13870
                                            13890
               13860
                                  13880
      13850
ASTCCTGGACAGTGAATGACATTCAGAAAWCAATTCTGARAGCCCTCGGCHCAGGCGCTWCCCTGGAGGAAATGATGACA
TSAGGACCTGTCACTTACTGTAAGTCTTTWGTTAAGACTYTCGGGAGCCGKGTCCGCGAWGGGACCTCCTTTACTACTGT
X S W T V N D I Q K X I L X A L G X G A X L E E H M T>
                        13950
                                  13960
                                            13970
                                                     13980
     13930
               13940
GCATGTCAGGGAGTGGGAGGCCCTRGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCCCMTTTGGAAAGGCCC
14080
                                            14050
                                                     14060
                        14030
     pol 931-960 (96)
TGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGAGRTTAAGATTGGAGGCCAACTGAWAGAAGCCCTCC
ACGGTTTGACGAGACCTTTCCGCTTCCGCGACACCAGTAGGTTCTTCTAAATTCTAACCTCCGGTTGACTWICTTCGGGAGG
A K L L W K G E G A V V I Q D X K I G G Q L X E A L>
                                                              14150
                                           14130
                                                     14140
                                  14120
     14090
               pol 61-90 (38)
spacers
                       env 360-389 (160) 14210
              1418C
     14170
GTCCTGGCTRTCGAGAGGTATCTGAAAGATCAAMAGYTTCTGGGAMTCTGGGGCTGTAGCGGAAAGGCTGCTATGGAAAACAGGCCGAYAGCTCTCCTATGAAAGATCACTTTTCTAGTTKTCRAAGACCCTKAGACCCCGACATCGCCTTTTCCGACGATACCTTTT
 V L A X E R Y L K D Q X X L G X W G C S G K A A M E N>
                                                    14300
                        14270
              14260
                                   vif 1-30 (100)
     14250
CAGATGGCAAGTGHTGATCGTCTGGCAAGTGGACAGGATGARGATTAGGACATGGAAWAGCCTCGTGAAACACCATATGY
GTCTACCGTTCACKACTAGCAGACCGTTCACCTGTCCTACTYCTAATCCTGTACCTTWTCGGAGCACTTTGTGGTATACR
 R W Q V X I V W Q V D R M X I R T W X S L V K H H M>
                                          env 390-419 (162) 14390
                                                                       14400
              14340
                       14350
                                 14360
A THITTATCTGTACCACARMCGTCCCCTGGAACTCCASCTGGAGCAATAAGTCCYTCGAAGAGATTTGGRATAACATGACC
TAKAATAGACATGGTGTYKGCAGGGGACCTTGAGGTSGACCTCGTTATTCAGGRAGCTTCTCTAAACCYTATTGTACTGG
  X I C T T X V P W N S X W S N K S X E E I W X N M T>
```

FIGURE 15 (Cont)

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14420 14430 vpu 16-45 (133) 14460 TGGATKSAATGCTGATTMTCGCTATCGTCGTCGTCGACCATTGYGTWTATCGAATACARGAAACTGCTCARGCAAAGGAR ACCTAMSTTACCGACTAAKAGCGATAGCAGCACCCTGGTAACRCAWATAGCTTATGTYCTTTGACGAGTYCGTTTCCTY W X X W L I X A I V V W T I X X I E Y X K L L X Q R X> 14520 gag 46-75 (4) 14490 14500 14510 14550 AATCGATAGGCTCATCRAAAGGCTCAACCCTGGCCTCCTGGAAACCKCTGAGGGATGTMAACAGATCCTGGRACAGCTCC TTAGCTATCCGAGTAGYTTTCCGAGTTGGGACCGGAGGACCTTTGGMGACTCCCTACAKTTGTCTAGGACCYTGTCGAGG
I D R L I X R L N P G L L E T X E G C X Q I L X Q L> 14610 14620 14630 14590 14600 14570 14580 AGYCCGCCCTCMAGACAGGCWCCGAAGAGCTCTTTTTGC AGAAAGCTCCTGARACAGAGAARGATTGACAGACTGATTRAG TCRGGCGGGAGKTCTGTCCGWGGCTTCTCGAGAGATGTTTCGAGGACTYTGTCTCTTYCTAACTGTCTGACTAAYTC XALXTGXEELS S R K L L X Q R X I D R L I X> 14700 vpu 31-60 (134) 14670 14680 14690 AGAAYCAGAGAGAGAGCCGAAGACTCCGGCAATGAGTCCGAGGGAGAGACACCCGGAATCAGATACCAATACAATGTGCT 14780 14770 14760 14730 pol 286-315 (53) CCCCCAAGGCTGGAAGGGCTCCCCASCCATTTTCCAAAGCTCCATGMCCMAAATCCTCATGATGCAAAGGGGGAAACTTTA GGGGGTTCCGACCTTCCCGAGGGGTSGGTAAAAGGTTTCGAGGTACKGGKTTTAGGAGTACTACGTTTCCCCTTTGAAAT
PQGWKGSPXIFQSSMXXILMMQRGNF> 14860 14820 gag 376-405 (26) 14810 RGGGACHGAANAGGATTRTCAAGTGCTTCAACTGTGGAAAGGAAGGCCATHTCGCTARGAATTGCAGACCTCCCCTGGAG YCCCTGRCTTTTCCTAAYAGTTCACGAAGTTGACACCTTTCCTTCCGGTAKAGCGATYCTTAACGTCTGGAGGGGACCTC X G X K R I X K C P N C G K E G H X A X N C R P P L E> 14900 14910 14940 14950 14960 14890 rev 76-105 (129) AGACTGMACCTGGATTGCTCCGAGGATWGCGRCACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGGAGTGGGA TCTGACKTGGACCTAACGAGGCTCCTAWCGCYGTGGAGGCCGTGTGTCGTTTCGGTTCCGTGTCTCTCTCACCCT R L X L D C S E D X X T S G T Q Q S Q G T E T G V G 15030 14970 14980 14990 15000 pol 781-810 (86) CGTGGCTGTGCATGTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTM GCACCGACACGTACACCGGTCGC:CTATATAGCTTCGGCTTCACTAGGGACGGCTTTGACCTGTCCTTTGGCGAATGAAAK V A V H V A S G Y I E A E V I P A E T G Q E T A Y F> 15050 15060 15070 15080 15090 env 200-229 (150) TCCTCAAGATTARGCCTGTGGTCAGCACACAGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGAARTCRTTATCAGAAGC AGGAGTTCTAATYCGGACACCAGTCGTGTGGGAGGACGAGTTGCCATCGGAGCGACTTCTCCTTYAGYAATAGTCTTCGX L K I X P V V S T Q L L N G S L A E E E X X I R S 15170 pol 406-435 (61) 15130 15150 15160 GAAAACYTTACCRATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACSCTGGCATCAAAGTGARGCAACT CTTTTGRAATGGYTATTGTTTGACCAGCCGTTTGACTTAACCCGAAGGGTTTAGATGSGACCGTAGTTTCACTYCGTTGA ENXTXNKLVGKLNWASQIYXGIKVXQL> . 15230 15280 15250 env 121-139 (145) 15210 15220 15240 GTGTAAGCTCCTGAGAGGCRCCAAAGCCCTCACCCCTCTGTGTGACACTGAATTGCACAAAACGCTAACCTCATCAATG CACATTCGAGGACTCTCCGYGGTTTCGGGAGTGGGGAGACACACACTGTGACTTAACGTGTTTGCGATTGGAGTAGCTAC C K L L R G X K A L T P L C V T L N C T N A N L I N> spacers 15310 15330 15320 tat 76-102 (123) TGAATGCTCCTCAAMCCAGAGGCGATAACCCTACCGRTCCCRAAGAGTCCAAGAARAGGTCGMGTCCAAGRCAGAGACA actt/cgacg/cttkggictccgctattgggatggcyagggyttctcaggttctttytccagckcaggttctgt AQXRG DNPTXPXESKKXVX SKXET>

FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

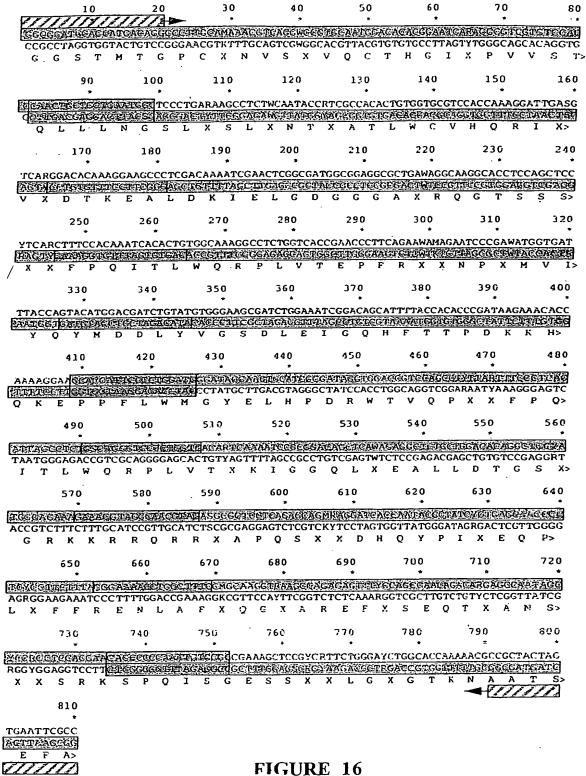
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15390
                                                         rev 61-90 (128)
 L E> join
  D P X D A A P S S X X L C R X A E P V P L Q L P P
                                                                                                         C6
                                                                                 15510
                                                                     15500
        15450
                . 15460
                                15470
                                             15480
                                                         15490
 AAGGCTCMACCTCGACTGTAGCGAAGACWGTGRCGMACTGGATAAGTGGGCCTCCCTGTGGAACTGGTTCRATATCWCCA
TTCCGAGKTGGAGCTGACATCGCTTCTGWCACYCCKTGACCTATTCACCCGGAGGGACACCTTGACCAAGYTATAGWGGT
R L X L D C S E D X X X L D K W A S L W N W F X I X>
                                                                                 15590
                               15550
                                            15560
                                                         15570
                                                                     15580
    env 450-479 (166)
 ASTGGCTGTGGTACATTAAGATTTCATTATGATTGTGGGAGGQAATAAGATTGTCAGGATGTACYHACCTGTCTCCATC
 TSACCGACACCATGTAATTCTAAAAGTAATACTAACACCCTCCGTTATTCTAACAGTCCTACATGRKTGGACAGAGGTAG
X W L W Y I K I F I M I V G G N K I V R M Y X P V S I>
                                                                     15660
                                           15640
                                                         15650
       15610
                   gag 271-300 (19)
 CTCGACATTARGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTGCCTAAGCTCCTGTGGAAGGGGAGAGGG
GAGCTCTAATYCGTTCCGGGATTCCTTGGGAAGTCCCTAATGCACCTGTCTAAGCGATTCGAGGGACACCTTCCCTCTCCC
L D I X Q G P K E P F R D Y V D R F A K L L W K G E G>
                                                        15730
                                                                     15740
                                                                                 15750
                   15700
                              pol 946-975 (97)
 AGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGGCTAAGATTATQGAACTGAATAAGAGAA
 TCGGCAGCACTAAGTCCTGTTGAGGCTGTAATTCCAGCACGGGTCCTCTTTCCGATTCTAATAGCTTGACTTATTCTCTT
A' V V I Q D N S D I K V V P R R K A K I I E L N K R>
                                                                                         spacers
                               15790
                                           pol 226-255 (49)
                                                                   15820
                   15780
 CCCAAGACTTTTGGGAAGTGCAACTGGGAATCCCTCACCCTGGTGACAAAAAAGAAAAAAGTCCGTGACAGTGGCCGCT
 GGGTTCTGAAAACCCTTCACGTTGACCCTTAGGGAGTGGGACGACCTGACTTTTTCTTTTTCAGGCACTCTCAQCGGCGA
 T Q D F W E V Q L G I P H P A G L K K K S V T V A
                                                        env 1-30 (137)
                                           15880
       15850
 ATGAGAGTGAAAGAGACACACATGAACTGGCCCAATCTGTGGARGTGGGGCACAMTGATTCTGGGAMTGGTCATSATTTG
 TACTCTCACTTTCTCTGTGTCTACTTGACCGGGTTAGACACCCTYCACCCCGTGTKACTAAGACCCTKACCAGTASTAAAC
 M R V K E T Q M N W P N L W X W G T X I L G X V X I C>
                                                        15970
                                           15960
                                                                  pol 421-450 (62)
                               15950
CTCCGCCTCQATTAAGGTCARACAGCTCTGCAAACTGCTCAGGGGTRCAAAGGCTCTGACAGASATTGTGHCACTGACAG
GAGGCGGAGGTAATTCCAGTYTGTCGAGACGTTTGACGAGTCCCCAYGTTTCCGAGACTGTCTSTAACACKGTGACTGTC
S A S I K V X Q L C K L L R G X K A L T X I V X L T>
                                                                  nef 181-196 (191)
                                                        16050
                              16030
                                           16040
      16010
AGGANGCCGAACTGCAACTGCTCAWATGGAAGTTTGACTCCCRCCTCGCCCKGAGACATATSGCCAGGGAACTGCRTCCC
TCCTTCGGCTTGACCTTGAGGGTWTACCTTCAAACTGAGGGYGGAGCGGGMCTCTGTATASCGGTCCCTTGACGYAGGG
E E A E L E L L X W K F D S X L A X R H X A R E L X P>
                                                                  env 570-599 (174) 16160
                    spacers
      16090 .
                                           16120
GAGTWETACAAAGACTGGGCTGETGTCGAGCTCCTGGGACRCTCCAGCCTCARGGGACTGCRAAGGGGATGGGAAGSCCT
CTCAWGATGTTTCTGACCCGACGACAGCTCGAGGACCCTGYGAGGTCGGAGTYCCCTGACGYTTCCCCTACCCTTCSGGA
E X Y K D C A A V E L L G X S S L X G L X R G W E X L>
                                                                   16220
                                           16200
                                                       16210
      16170
                  16180
                              16190
CAAGTATTKGKGGAACCTCCTGCWGTATTGGGGTTCTTGGGCTTGGGCGAACTGCAAYCTGCTCTGMAAACCGGAWCAGAGG
GTTCATAAMCMCCTTGGAGGACGWCATAACCCCCTGGATCGGACCYCGTTGACGTTRGACGAGACKTTTGGCCTWGTCTCC
                                                                                                      C6
                                                                                                     join
  K Y X X N L L X Y W G S S L X Q L Q X A L X T G X E>
                                                                                                      C7
                                                                   16300
                                                                                16310
                              16270
                                           16280
                                                        16290
     gag 61-90 (5)
AACTGARGTCCCTGTWTAACACARTCGCTACCCTCTGGTGTGTGCATCACGACGTCTACAAATACAAAGTGGTCRAAATC
TTGACTYCAGGGACAWATGTGTYAGCGATGGAGACCACACACGTAGTCCTCGAGATGTTTATGTTTCACCAGYTTTAG
E L X S L X N T X A T L W C V H Q E L Y K Y K V V X I>
```

FIGURE 15 (Cont)

```
16370
                                                                        16380
                                                                                    16390
                                               16360
                   env 270-299 (154)
   RAACCCCTCGGCRTTGCCCCTACCARAGCCAAAAGGAGAGTGGTCSAGAGAGAGAAAAGGCTCACCGAWATCGTCMCACT
   YTTGGGGAGCCGYAACGGGGATGGTYTCGGTTTTCCTCTCACCAGSTCTCTCTTTTCGGAGTGGCTWTAGCAGKGTGA
X P L G X A P T X A K R R V V X R E K R L T X I V X L>
                                                                                                16480
                                                           16450
                                                                       16460
                                                                                    16470
                     16420
                                 pol 436-465 (63)
         16410
  CACCGAAGAGGCTGAGCTGGAGCTGGMGGAAAACAGAGAGATTCTGARGGAACCCGTCCACGGAGTGTAT
   GTGGCTTCTCCGACTCGACCKCCTTTTGTCTCTCTAAGACTYCCTIGGGCAGGTGCCTCACATATCTCACGAGC
T E E A E L E L X E N R E I L X E P V H G V Y R V L>
                                                                                    16550
                                                                                                16560
                                             gag 361-390 (25)
         16490
                     16500
                                  1.6510
  CCGAAGCCATGAGCCAAGYCAMCMATGCCAACATCATGATGCAGAGAGGCAATTTCARAGGCCMAAAGAGAATCRTCAAA
  GGCTTCGGTACTCGGTTCRGTKGKTACGGTTGTAGTACTACGTCTCTCCGTTAAAGTYTCCGGKTTTCTCTTAGYAGTTT
  A E A M S Q X X X A N I M M Q R G N F X G X K R I X K>
        16570
                     16580
                                 16590
                                              16600
                                                          nef 61-90 (183)
  CAAGAGGAAGAGGRGGTCGGCTTCCCCGTCAGGCCTCAGGTCCCACTGAGACCTATGACCTACAAAGSAGCCRTCGATCT
  GTTCTCCTTCTCCYCCAGCCGAAGGGGCAGTCCGGAGTCCAGGGTGACTCTGGATACTGGATGTTTCSTCGGYAGCTAGA
Q E E E X V G F P V R P Q V P L R P M T Y K X A X D L>
                                                          16690
                    16660
                                 16670
                                              16680
                                                                     gag 286-315 (20)
  GTCCYTCTTCARACAGGCACCCAAAGAGCCTTTCAGAGACTATGTGGATAGGTTTTWCAAAACCCTCAGGGCTGAGCAAG
  CAGGRAGAACTYTGTCCCTGGGTTTCTCGGAAAGTCTCTGATACACCTATCCAAAAWGTTTTGGGAGTCCCGACTCGTTC
S X F X Q G P K E P F R D Y V D R F X K T L R A E Q>
                                                         16770
                                             16760
                                 16750
                                                                       gag 16-45 (2)
 CCWCACAGGAWGTGAAAAATTGGGAGAAAATCAGACTGAGACCTGGTGGCAAAAAGAAATACARAMTGAAACACWTTGTG
 GGWGTGTCCTWCACTTTTTTGACCCTCTTTTAGTCTGACTCTGGACCACCGTTTTTCTTTATGTYTKACTTTGTGKAACAC
                                                         16850
                                16830
                                             16840
                    16820
        16810
                                                                      pol 646-675 (77)
 TGGGCCTCCAGGGAACTGGAAAGGITTGCCTCCCAGTATGCCCTCGGCATCATCCWAGCCCAACCCGATARGTCCGAGTCACCCGGAGGTCCCTTGACCTTTTCCAAACCGAGGGTCATACGGGAGCCGTAGTAGGWTCGGGTTGGGCTATYCAGGCTCAG
W A S R E L E R F A S Q Y A L G I I X A Q P D X S E S>
                                                                     16940
                                                         16930
                                16910
                                             16920
        16890
                    16900
 CGAGSTCGTGARTCAGATTATCGAAVAGCTCATCAAGAACAATTCCCGTCGCCGRAKSGACAGARCAGARTCATTGAGGTCG
GCTCSAGCACTYAGTCTAATAGCTTBTCGAGTAGTTCTTCTTAACGGCAGCGGCYTMCCTGTCTGTCTYAGTAACTCCAGC
E X V X Q I I E X L I K K I A V A X X T D R X I E V>
                                                                     17020
                                                                                  17030
     env 615-644 (177)
                               16990
                                             17000
                                                         17010
 YCCAAAGGGCTKGGAGAGCCATTCTGMATATCCCCASGAGAATCAGACAAGAGAGCCCCGGAAGGTGGCCCGTCARGRGTTTCCCGAMCCTCTCGGTAAGACKTATAGGGGTSCTCTTAGTCTGTTGATCTGACCGGCCCTTCCACCGGCCAGTYC
                                                                                                        C7
                                                                                                       join
 X Q RAXRAIL X I P X R I R Q T R L A G R W P V X>
                                                                                                        C8
                                            17080
                                                         17090
                                                                     17100
                                                                                  17110
                                                                                              17120
                   pol 811-840 (88)
 RYAATCCATACCGATAACGGAAGCAATTTCACAAGCRCTRCCGTCAAGGCTGCCTGCTGGTGGGCTGATGTGARACAGCT
 YRTTAGGTATGCCTATTGCCTTCGTTAAAGTGTTCGYGAYGGCAGTTCCGACGGACGACCACCCGACTACACTYTGTCGA
X I H T D N G S N F T S X X V K A A C W W A D V X Q L>
                                                                                 17190
                                                                                            spacers
                                                                     17180
                   17140
                                                        17170
       17130
                               pol 511-540 (68)
 CACCGMAGYCGTCCAGAAARTCGCTACCGAAAGCATTGTGATATGGGGAAAGACACCCAAGTTCARACTGCCTATQGCTG
 GTGGCKTCRGCAGGTCTTTYAGCGATGGCTTTCGTAACACTATACCCCTTTCTGTGGGTTCAAGTYTGACGGATAQCGA
   T X X V Q K X A T E S I V I W G K T P K F X L P I A>
                                  spacers
                                                 Bglll EcoRl
CCGCCAGCAACGAGAACATGGASRCCATCGCTGCTTGAAGATCTGAATTTGCC
GCCGCTCGTTGCTCTTGTACCTSYGGTACGACGAACTTCTAGACTTAACGG
A S N E N M X X M A A R S E F A>
        Flu NP epi (Mouse)
                                           Stop
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FIGURE 15 (Cont)

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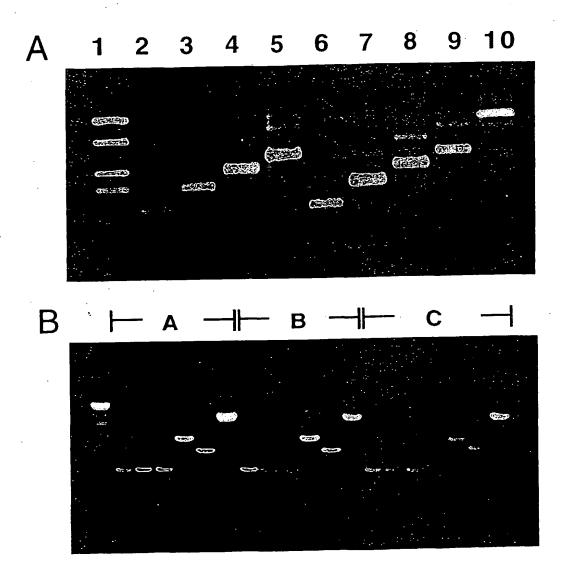


FIGURE 17

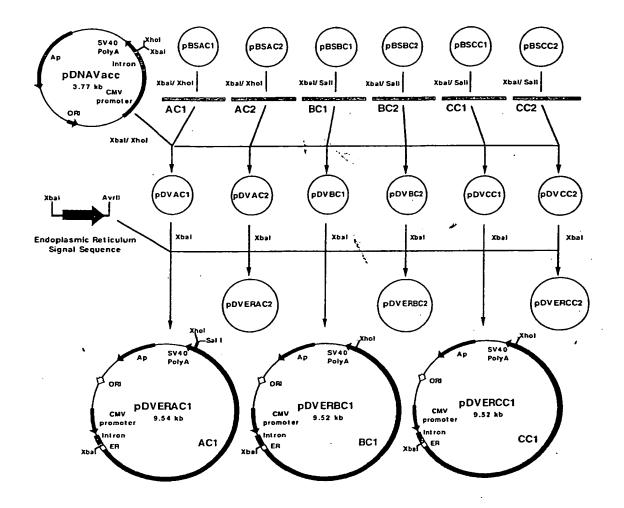
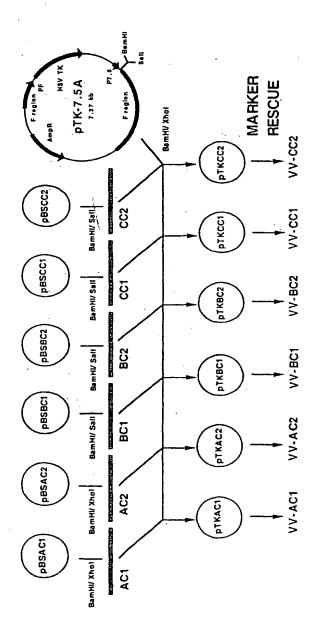


FIGURE 18A



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FIGURE 18B

WO 01/090197 PCT/AU01/00622

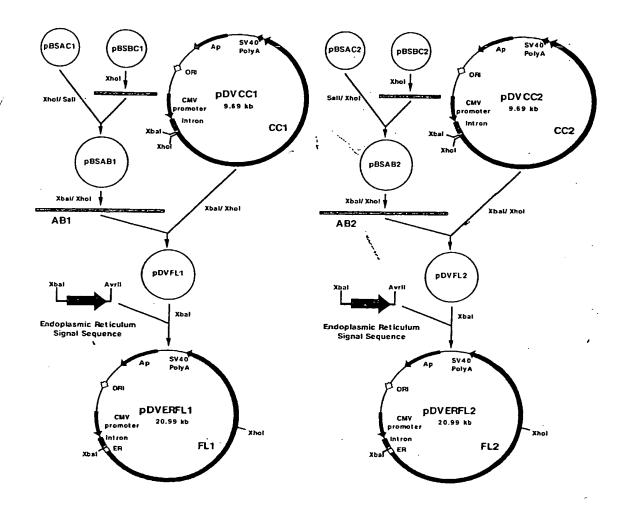
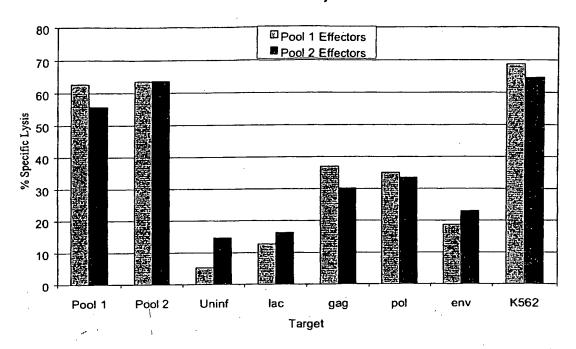


FIGURE 18C

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# Subject1



# Subject2

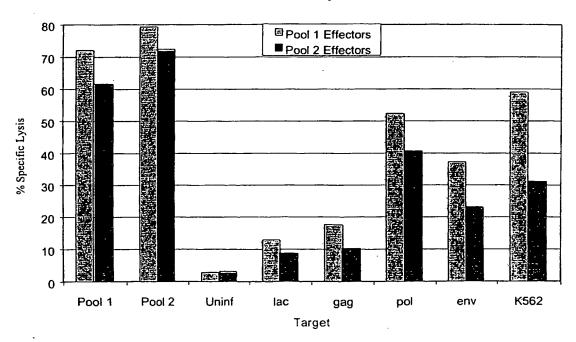


FIGURE 19

WO 01/090197

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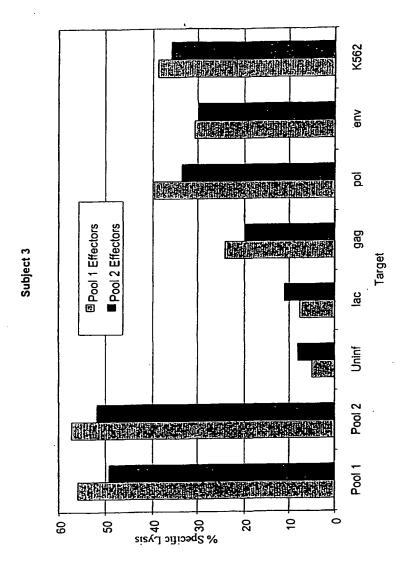


FIGURE 19 (Cont)

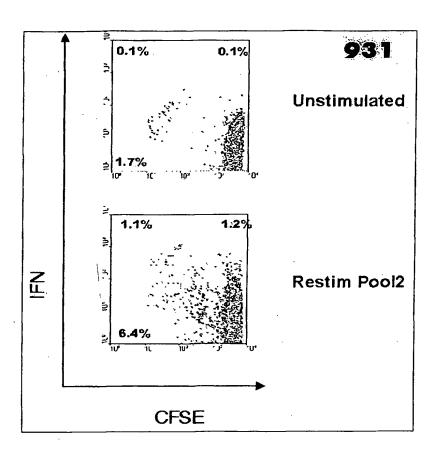


Figure 20

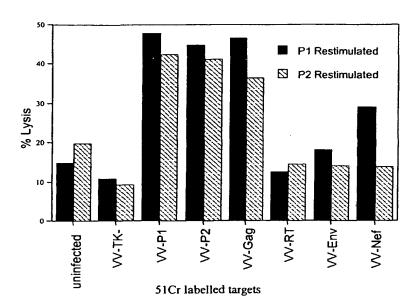


Figure 21

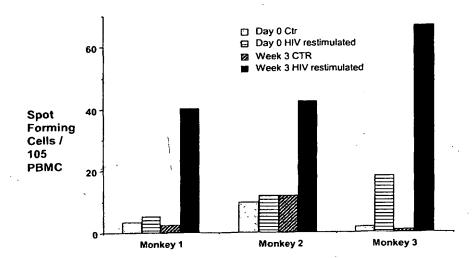


Figure 22A

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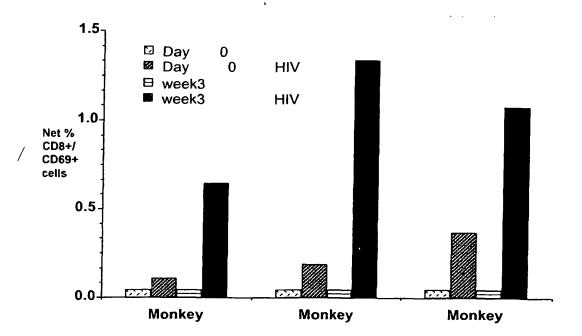


Figure 22B

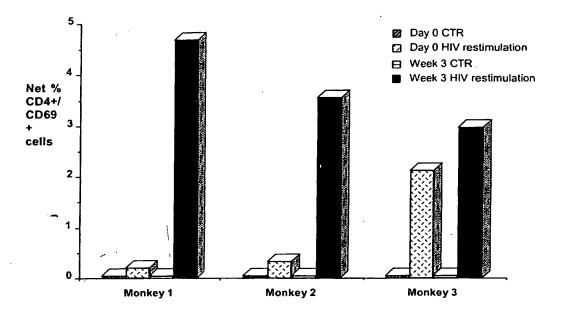


Figure 22C

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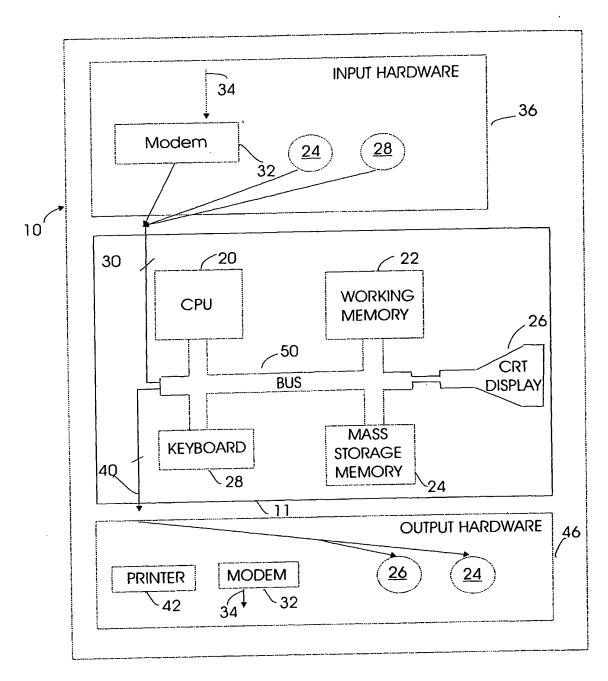


FIGURE 23

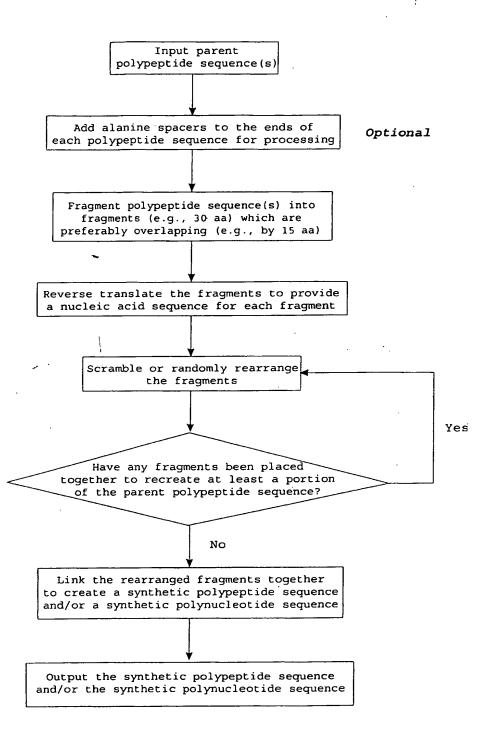


Figure 24

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```
/* Scramble */
                                                95/216
 /* Includes */
 #include <stdio.h>
 #include <stdlib.h>
 #include <string.h>
 #include <time.h>
 /* Constant definitions */
 /* Version Information */
#define VERSION NO
                                                                 "0.2"
 #define VERSION DATE
                                                      "04/03/1999"
/* Misc */
#define KEYBOARD_BUFFER_SIZE
                                           256
                                                                 /*size of keyboard read buffer */
#define LEN_CODON
                                                                            /*length of codon (including
null) */
#define BUFFER_SIZE
                                                                 10000
                                                                            /*size of file read buffer */
#define TRUE
                                                                                       /*boolean true */
#define FALSE
                                                                 0
                                                                                       /*boolean false */
/* Error codes */
#define E_NOERROR
                                                      0
                                                                            /*no error */
#define E_NOINFILE
#define E_MALLOC
                                                      1
                                                                            /*genes file not found */
                                                      2
                                                                            /*memory allocation error */
#define E_FILEREAD
                                                      3
                                                                            /*file read error */
#define E_CREATE_OUTPUT_FILE
                                                                 /*error creating output file */
#define E_OVERLAP
                                                                           /*segment overlap >= length
/* Structure definitions */
typedef struct gene GENE;
typedef GENE * P_GENE;
typedef struct gene_segment GENE_SEGMENT;
typedef GENE_SEGMENT * P_GENE_SEGMENT;
struct gene {
          char * name;
          char * data;
          P_GENE next_gene;
};
struct gene_segment {
          P_GENE p_gene;
          int number;
          int offset;
          int first_codon_choice;
          char * amino data;
          char * dna_data;
          P_GENE_SEGMENT next_seg;
};
```

```
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 /* Function prototypes */
 int prolog();
 int get_parameters();
 int read_int(char * prompt);
 int load_genes();
 int add_gene(char * gene_name,char * gene_data);
 void insert_gene(P_GENE * head,P_GENE new_gene);
 int add_aa();
 int split_genes();
int split_gene(P_GENE g);
int insert_segment(P_GENE_SEGMENT * head_seg,P_GENE_SEGMENT new_seg);
 int convert_segments_aa_to_dna();
 int convert aa to dna(char * aa ptr,char * dna ptr,int first_choice);
 char * codon(char acid_char,int preferred);
 int perform_scramble();
 int scramble_segments();
 int adjacent_segments();
 int display_genes();
 int write_output_file();
void strip_newline(char * strip_str);
void pad_amino_string(char * amino_ptr, char * padded_ptr);
 int even(int test_num);
 void read_str(char * prompt,char * string);
char * read_nonblank_line(char * buf,int buf_size,FILE * in_file);
int user_confirmation();
void test();
/* Global variables */
char * codon_table[26][2] = {
/* A 00 */ {"GCC","GCT"},
/* - 01 */ {"???","???"},
/* C 02 */ {"TGC","TGT"},
/* D 03 */ ("GAC","GAT"),
/* E 04 */ ("GAG","GAA"),
/* F 05 */ ("TTC","TTT"),
/* G 06 */ {"GGC","GGA"},
/* H 07 */ {"CAC","CAT"},
/* 108 */ {"ATC","ATT"},
/* - 09 */ {"????","???"},
/* K 10 */ {"AAG","AAA"},
/* L 11 */ {"CTG","CTC"},
/* M 12 */ {"ATG","ATG"},
/* N 13 */ ("AAC", "AAT"),
/* - 14 */ ("???","???"),
/* P 15 */ {"CCC","CCT"},
/* Q 16 */ {"CAG","CAA"},
/* R 17 */ {"AGG","AGA"},
/* S 18 */ {"AGC","TCC"},
/* T 19 */ {"ACC","ACA"},
/* - 20 */ {"???","???"},
/* V 21 */ {"GTG","GTC"}
/* W 22 */ {"TGG", "TGG"},
```

Figure 25 (Cont)

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```
/* - 23 */ {"???","???"},
/* Y 24 */ {"TAC","TAT"},
/* - 25 */ {"???","???"}
                                                     97/216
char * error_text[] = {
/* 01 */ ,"ERROR: Input file not found!"
/* 02 */ ,"ERROR: Memory allocation error"
/* 03 */ ,"ERROR: File read error"
/* 04 */ ,"ERROR: Could not create output file"
/* 05 */ ,"ERROR: Segment overlap must be less than segment length"
char disease_name[KEYBOARD_BUFFER_SIZE];
char input file name[KEYBOARD BUFFER SIZE];
char output_file_name[KEYBOARD_BUFFER_SIZE];
int num_genes = 0;
int num_segments = 0;
int len_segment;
int segment_overlap;
P_GENE first_gene = NULL;
P_GENE_SEGMENT first_segment = NULL;
P_GENE_SEGMENT * scrambled_segments = NULL;
/* Mainline */
void main() {
           int error = E NOERROR;
           printf("Scramble - Version %s, %s\n\n", VERSION NO, VERSION DATE);
           /* Initial processing */
           if (!error)
                       error = prolog();
           /* Get various program parameters from user */
           if (!error)
                       error = get parameters();
           /* Load genes from genes file */
           if (!error)
                       error = load_genes();
           /* Add 'AA' to start and end of all genes */
           if (!error)
                       error = add_aa();
           /* Split genes into overlapping chunks */
           if (!error)
                       error = split_genes();
          /* Convert segment amino acid to dna */
          if (!error)
                       error = convert_segments_aa_to_dna();
```

Figure 25 (Cont)

```
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           /* Scramble the segments */
           if (!error)
                       error = perform_scramble();
           /* Write output file */
           if (!error)
                       error = write_output_file();
           /* Show error if there was one */
           if (error)
                       printf("%s\n",error_text[error]);
/* prolog() */
/* Perform any initial processing required */
int prolog() {
           /* Seed the random number generator, using the system clock */
           /* Don't run the program more than once in the same second! */
           /* Or we'll get the same randomisation!!!!!!!!!!!!!!! */
            srand(time(NULL));
           return E_NOERROR;
}
/* get_parameters() */
/* Ask for various parameters from the user (stdin) */
     Disease name
     Input file name
     Output file name
     Segment length
int get_parameters() {
            int valid;
            read_str("Enter disease name
                                              : ",disease_name);
            read_str("Enter input file name : ",input_file_name);
read_str("Enter output file name : ",output_file_name);
            valid = FALSE;
            while (!valid) {
                        len_segment = read_int("Enter segment length : ");
                        if (len_segment % 2)
                                    printf("Segment length must be even!\n");
                        else
                                    valid = TRUE;
            segment_overlap = len_segment / 2;
            return E_NOERROR;
/* load_genes() */
```

Figure 25 (Cont)

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```
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/* Load the genes from the input file */
int load_genes() {
     FILE * input_file;
           char name buf[BUFFER_SIZE];
           char data buf[BUFFER SIZE];
           /* Open genes file for reading */
           if (NULL == (input file = fopen(input file name, "r")))
                     return E_NOINFILE;
           printf("Loading genes from: %s\n",input_file_name);
           num_genes = 0;
           /* Read gene name */
           while (NULL != read_nonblank_line(name_buf,BUFFER_SIZE,input_file)) {
                     /* Read the gene data */
                      if (NULL != read_nonblank_line(data_buf,BUFFER_SIZE,input_file)) {
                                 /* Allocate memory for new gene and add to list */
                                 if (rc = add_gene(name_buf,data_buf))
                                            break;
                     }
           /* Close genes file */
           fclose(input_file);
           return rc;
}
/* add _gene() */
/* Allocate memory for new gene, then insert in list */
int add gene(char * gene name,char * gene data) {
           P_GENE new_gene;
           /* Allocate storage for new gene */
           if (NULL == (new_gene = malloc(sizeof(GENE))))
                     return E_MALLOC;
           /* Initialise new gene */
           new_gene->next_gene = NULL;
           /* Allocate storage for gene name (+1 for null) */
           if (NULL == (new_gene->name = malloc(strlen(gene_name)+1)))
                     return E MALLOC;
          /* Store gene name */
          strcpy(new_gene->name,gene_name);
          /* Allocate storage for gene data (+1 for null) */
          if (NULL == (new_gene->data = malloc(strlen(gene_data)+1)))
                      return E_MALLOC;
          /* Store gene data */
          strcpy(new_gene->data,gene_data);
           /* Insert the new gene into linked list */
           insert_gene(&first_gene,new_gene);
          /* Increment num_genes */
          num_genes++;
```

Figure 25 (Cont)

```
100/216
          return E_NOERROR;
/* insert gene() */
/* Insert gene into linked list */
void insert_gene(P_GENE * head_gene,P_GENE new_gene) {
          P GENE * cur_ptr = head_gene;
          while (NULL != (*cur_ptr))
                     cur_ptr = &((*cur_ptr)->next_gene);
          *cur_ptr = new_gene;
}
/* add aa() */
/* Add 'AA' to the start and end of every gene */
char * new_data;
          while (NULL != cur_gene) {
                     /* Allocate storage to fit the gene plus four characters */
                     new_data = malloc(strlen(cur_gene->data)+5);
                     /* Shift gene data to new storage, add "AA" */
                     strcpy(new_data,"AA");
                     strcat(new_data,cur_gene->data);
                     strcat(new_data,"AA");
                     /* Free previous gene data storage */
                     free(cur_gene->data);
                     /* Set gene data pointer to new storage */
                     cur_gene->data = new_data;
                     /* Advance to next gene */
                     cur_gene = cur_gene->next_gene;
          }
          return E NOERROR;
/* split_genes() */
/* Split the genes into overlapping segments */
int split genes() {
          P_GENE cur_gene = first_gene;
          P_GENE_SEGMENT cur_seg = first_segment;
          printf("Splitting genes into segments...\n");
          /* Split the genes into segments */
          while (NULL != cur_gene) {
                     /* Split the gene */
                     split gene(cur_gene);
                     /* Advance to next gene */
```

Figure 25 (Cont)

```
cur_gene = cur_gene->next_gene;
           }
           /* Count the number of segments */
           num segments = 0;
           cur_seg = first_segment;
           while (NULL != cur_seg) {
                     num segments++;
                     cur_seg = cur_seg->next_seg;
          return E_NOERROR;
/* split_gene() */
/* Split a gene into overlapping segments */
int split_gene(P_GENE g) {
          char * seg_ptr;
          char * seg_buf;
P_GENE_SEGMENT new_segment = NULL;
          int done;
          int seg_ctr = 0;
          /* Allocate memory for segment buffer */
          if (NULL == (seg_buf = malloc(len_segment+1)))
                     return E_MALLOC;
          /* Insert a null at the end of the segment buffer, */
          /* so we can use it as a string */
          seg_buf[len_segment] = '\0';
          /* Set segment pointer to start of gene data */
          seg_ptr = g->data;
          done = FALSE;
          while (!(done)) {
                     /* So we know if we copied data */
                    seg_buf[0] = '\0';
                    /* Copy a segment of gene data to the segment buffer */
                    memcpy(seg_buf,seg_ptr,len_segment);
                    /* If there was some gene data copied to the buffer */
                    if (NULL != seg_buf[0]) {
                               /* Allocate storage for a new segment */
                               if (NULL == (new_segment = malloc(sizeof(GENE_SEGMENT))))
                                          return E_MALLOC;
                               /* Increment segment counter */
                               seg ctr++;
                               /* Setup the new segment */
                               new_segment->p_gene = g;
                               new segment->number = seg ctr;
                               new_segment->offset = seg_ptr - g->data + 1;
                               new_segment->next_seg = NULL;
```

Figure 25 (Cont)

```
if (NULL == (new_segment->amino_data = malloc(len_segment+1)))
                                           return E MALLOC;
                                 if (NULL == (new_segment->dna_data = malloc(len_segment*3+1)))
                                           return E MALLOC;
                                 new_segment->amino_data[0] = 10;
                                 new_segment->dna_data[0] = '\0';
                                 /* Copy segment data from buffer to new segment */
                                 strcpy(new_segment->amino_data,seg_buf);
                                 /* Insert new segment into chain from gene */
                                 insert_segment(&first_segment,new_segment);
                      /* If we didn't read a full segment, we are finished! */
                      if (strlen(seg_buf) < len_segment)
                                done = TRUE;
                      /* Otherwise, advance segment pointer to next segment in buffer */
                                 seg_ptr = seg_ptr + len_segment - segment_overlap;
          }
/* insert_segment() */
/* Insert a segment node at the end of the list */
int insert_segment(P_GENE_SEGMENT * head_seg,P_GENE_SEGMENT new_seg) {
          P GENE SEGMENT * cur_ptr = head_seg;
          while (NULL != (*cur_ptr))
                     cur_ptr = &((*cur_ptr)->next_seg);
          *cur_ptr = new_seg;
/* convert segments aa to_dna */
/* Go thru segments, and for each, convert amino acids to dna */
int convert_segments_aa_to_dna() {
          P_GENE_SEGMENT cur_seg = first_segment;
          int first choice = 1;
          int alternate;
          printf("Converting to DNA...\n");
          /* Work out if we need to alternate the first codon choice or not */
          /* Don't need to do this anymore, since the segment length is
          /* forced to be even, and the overlap is half the length (odd). */
          /*alternate = ((even(len_segment) && even(segment_overlap))
                                || (!even(len_segment) && !even(segment_overlap)));*/
          alternate = FALSE;
          while (NULL != cur_seg) {
                     cur_seg->first_codon_choice = first_choice;
                     convert_aa_to_dna(cur_seg->amino_data,cur_seg->dna_data,
                                                                           cur seg->first_codon_choice);
```

```
/* Address next segment */
                        cur_seg = cur_seg->next_seg;
                        /* If we are alternating, alternate the first codon choice */
                        /*if (alternate)
                                    if (1 == first_choice)
                                               first_choice = 2;
                                   else
                                               first_choice = 1;*/
            }
            return E_NOERROR;
 }
 /* convert_aa_to_dna */
 /* Converts a string of amino acid to dna */
 /* NOTE: assumes that buffer at dna_ptr is large enough to hold dna!!! */
 int convert_aa_to_dna(char * aa_ptr,char * dna_ptr,int first_choice) {
            char * p_codon;
            int cur_preferred = first_choice;
            while ('\0' != *aa_ptr) {
                       p_codon = codon(*aa_ptr,cur_preferred);
                       strcat(dna_ptr,p_codon);
                       "/" If we didn't find a codon, log a warning */
                       if (0 == strcmp(p\_codon,"???\0"))
                                   printf("WARNING: no codon found for amino acid!\n");
                       /* Alternate current preferred codon */
                       if (1 == cur_preferred)
                                  cur_preferred = 2;
                       else
                                   cur_preferred = 1;
                       aa_ptr++;
           return E_NOERROR;
/* codon */
/* Returns a pointer to a codon corresponding to the amino acid passed */
/* The codon pointer is to 3 characters, plus a terminating null */
char * codon(char acid_char,int preferred) {
           int codon_table_index;
           char * codon ptr;
           /* Determine index into codon_table (table starts at 'A') */
           codon_table_index = acid_char - 'A';
           /* Set pointer to appropriate codon */
           codon_ptr = codon_table[codon_table_index][preferred-1];
```

```
return codon_ptr;
/* display_genes() */
/* Display the name and data for all genes */
int display_genes() {
            P_GENE cur_gene = first_gene;
            while (NULL != cur_gene) {
                       printf("%s\n",cur_gene->name);
printf("%s\n",cur_gene->data);
                       cur_gene = cur_gene->next_gene;
           return E_NOERROR;
}
  perform_scramble() */
/* Scramble the segments */
/* Check for adjacent segments. If there are, rescramble */
int perform_scramble() {
           int done = FALSE;
           int rc = E NOERROR;
           while (TRUE) {
                       rc = scramble_segments();
                       if (E_NOERROR == rc)
                                   if (adjacent_segments()) {
                                              printf("Adjacent segments detected! Rescramble? (y/n) ");
                                              if (!user_confirmation()) {
                                                          printf("WARNING: Adjacent segments in output
file.\n");
                                   }
                                   else
                                              break;
                       else
                                   break;
           return rc;
/* scramble segments() */
/* Randomly scramble the segments, putting pointers in scrambled_segments[] */
int scramble_segments() {
     P_GENE_SEGMENT cur_seg = first_segment;
     int i,j;
}
           P GENE SEGMENT temp;
           printf("Scrambling segments...\n");
```

Figure 25 (Cont)

```
/* Allocate storage for array of segment pointers */
            if (NULL == (scrambled_segments = malloc(sizeof(P_GENE_SEGMENT)*num_segments)))
                        return E MALLOC;
            /* First, initialise scrambled_segments in same order as linked list */
            while (cur_seg != NULL) {
                        scrambled_segments[i] = cur_seg;
                        cur_seg = cur_seg->next_seg;
            }
            /* Now, randomly scramble the segments */
            for (i=0;i<num_segments;i++) {
                                     = rand() % num_segments;
                                        = scrambled_segments[i];
                       scrambled_segments[i] = scrambled_segments[j];
                       scrambled_segments[j] = temp;
            return E NOERROR;
}
/* adjacent_segments() */
/* Determine if the scrambled segment order has resulted in */
/* two segments which were adjacent originally (ie every
/* second one) have ended up adjacent.
int adjacent_segments() {
           int i;
           int rc = 0;
           P_GENE_SEGMENT cur_seg;
P_GENE_SEGMENT next_seg;
           for (i=0;i<num segments-1;i++) {
                       /* Address current and next segments */
                       cur_seg = scrambled_segments[i];
next_seg = scrambled_segments[i+1];
                       /* Do segments come from same gene, and are two apart? */
                       if (((cur seg->p gene == next_seg->p gene)
                                  && ((cur_seg->number == (next_seg->number)+2)
                                             || (cur_seg->number == (next_seg->number)-2))))
                                  return 1;
           return 0;
/* write_output_file() */
/* Write out segments (in initial non-scrambled order) */
/* Write out synthetic protein (in scrambled order) */
/* Write out synthetic dna (in scrambled order) */
int write_output_file() {
           FILE * output_file;
```

```
char * amino_buffer;
P GENE SEGMENT cur_seg;
/* Open output file for writing (erase any contents) */
if (NULL == (output_file = fopen(output_file_name, "w")))
             return E_CREATE_OUTPUT_FILE;
/* Allocate memory for padded amino string buffer */
if (NULL == (amino_buffer = malloc(len_segment*3+1)))
             return E MALLOC;
printf("Writing output file: %s\n",output_file_name);
/* Write output file header information */
fprintf(output_file,"Scramble %s - Output File\n",VERSION_NO);
fprintf(output file,"\n");
                                        : %s\n",disease_name);
fprintf(output_file,"Disease name
fprintf(output_file;"Input filename : %s\n",input_file_name);
fprintf(output_file,"Output filename : %s\n",output_file_name);
fprintf(output_file,"Number genes : %d\n",num_genes);
fprintf(output_file,"Number segments : %d\n",num_segments);
fprintf(output_file,"Segment length : %d\n",len_segment);
fprintf(output_file,"Segment overlap : %d\n",segment_overlap);
/* Write out segments in initial non-scrambled order */
fprintf(output_file,"\n");
fprintf(output_file,"Segments in original order:\n");
fprintf(output_file,"-----\n");
cur_seg = first_segment;
while (NULL != cur_seg) {
             /* Format amino data to line up with codons */
             pad_amino_string(cur_seg->amino_data,amino_buffer);
fprintf(output_file,"Gene : %s\n",cur_seg->p_gene->name);
             fprintf(output_file,"Gene : %s\n",cur_seg->p_gene->na
fprintf(output_file,"Segment# : %d\n",cur_seg->number);
             fprintf(output_file,"Offset : %d\n",cur_seg->offset);
             fprintf(output_file,"1st Codon: %d\n",cur_seg->first_codon_choice);
fprintf(output_file,"%s\n",amino_buffer);
fprintf(output_file,"%s\n",cur_seg->dna_data);
             fprintf(output file,"\n");
             cur_seg = cur_seg->next_seg;
/* Write out segment names in scrambled order */
fprintf(output_file, "Segments in scrambled order:\n");
fprintf(output_file,"---
for (i=0;i<num_segments;i++) {
             /* Format amino data to line up with codons */
             pad_amino_string(scrambled_segments[i]->amino_data,amino_buffer);
             /* Write segment details */
             fprintf(output_file,"%s #%d\n",scrambled_segments[i]->p_gene->name,
                          scrambled_segments[i]->number);
             fprintf(output_file,"%s\n",amino_buffer);
fprintf(output_file,"%s\n",scrambled_segments[i]->dna_data);
             fprintf(output_file,"\n");
```

```
/* Write synthetic protein in one long string */
             fprintf(output_file,"Synthetic Protein:\n");
fprintf(output_file,"-----\n");
             for (i=0;i<num_segments;i++)
                         fprintf(output_file,"%s",scrambled_segments[i]->amino_data);
             fprintf(output_file,"\n\n");
             /* Write synthetic dna in one long string */
             fprintf(output_file,"Synthetic DNA:\n");
             fprintf(output_file,"----\n");
             for (i=0;i<num_segments;i++)
                         fprintf(output file,"%s",scrambled_segments[i]->dna_data);
             return E_NOERROR;
 }
 /* strip newline() */
 /* Replace the first newline character with a null */
 void strip_newline(char * strip_str) {
            char * newline_pos;
            /* Find the newline char */
            newline pos = strchr(strip str,'\n');
            /* If we found one, replace it with a null */
            if (NULL != newline_pos)
                        newline_pos[0] = '\0';
}
/* pad amino string */
/* Copy amino chars from amino_ptr to padded_ptr, padding each */
/* side with a space. */
void pad_amino_string(char * amino_ptr, char * padded_ptr) {
            while ('\0' != *amino_ptr) {
                        *padded_ptr = ' ';
                        padded_ptr++;
                        *padded_ptr = *amino_ptr;
                        padded ptr++;
                        *padded_ptr = ' ';
                        padded_ptr++;
                        amino_ptr++;
            }
            /* Stick a null at the end of the padded string */
            *padded_ptr = '\0';
/* even() */
/* True if test_num is even, otherwise false */
```

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```
int even(int test_num) {
            return !(test_num % 2);
/* Read an integer from stdin. Keep trying until valid int > 0 entered. */
/* Return the integer read, or 0 if error reading from stdin. */
int read_int(char * prompt) {
            char buffer[KEYBOARD_BUFFER_SIZE];
            int value_read;
            int valid = FALSE;
            while (!valid) {
                       printf("%s",prompt);
valid = TRUE;
                       fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
                       if (1 != sscanf(buffer, "%d", &value_read))
                                  valid = FALSE;
                       if (valid && (value_read < 1))
                                  valid = FALSE;
                       if (!valid)
                                  printf("Positive integer value please!\n");
           return value_read;
}
/* read_str() */
/* Read a string from the user (stdin) */
/* Strip the newline from it */
printf(prompt);
           fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
           sscanf(buffer, "%s", string);
}
/* read nonblank line() */
/* Read a line from file until we get a non-blank one */
char * read_nonblank_line(char * buf,int buf_size,FILE * in_file) {
           char * return_ptr;
           /* Read lines until we get a non-black one, or EOF */
           do
                      return_ptr = fgets(buf,buf_size,in_file);
           while ((NULL != return_ptr) && (("\n' == buf[0]) || (' ' == buf[0])));
           /* If we got a line, change the newline char to a null */
           if (NULL != return_ptr)
                      strip_newline(buf);
```

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```
return return_ptr;
/* user_confirmation() */
/* Read input from user. If user types 'y', return 1, otherwise 0 */
 int user_confirmation() {
                char buffer[KEYBOARD_BUFFER_SIZE];
                fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
if (('y' == buffer[0]) || ('Y' == buffer[0]))
                               return 1;
                else
                               return 0;
}
/* test() */
/* For debugging/development */
void test() {
               char str[100];
               printf("Enter something: ");
fgets(str,100,stdin);
               printf("line1\n");
printf("%s";str);
printf("line2\n");
               fgets(str,100,stdin);
}
```

#### 110/216

HepC Savine design

HepC la consensus polyprotein sequence used for scramble program

MSTNPKPQRKTKRNTNRRPQDVKFPGGGQIVGGVYLLPRRGPRLGVRATRKTSERSQPRGRRQPIPKARRPEGRTWAQ PGYPWPLYGNEGCGWAGWLLSPRGSRPSWGPTDPRRRSRNLGKVIDTLTCGFADLMGYIPLVGAPLGGAARALAHGVR VLEDGVNYATGNLPGCSFSIFLLALLSCLTVPASAYQVRNSTGLYHVTNDCPNSSIVYEAADAILHTPGCVPCVREGN ASRCWVAMTPTVATRDGKLPATQLRRHIDLLVGSATLCSALYVGDLCGSVFLVGQLFTFSPRRHWTTQGCNCSIYPGH ITGHRMAWDMMNWSPTAALVMAOLLRIPOAILDMIAGAHWGVLAGIAYFSMVGNWAKVLVVLLLFAGVDAETHVTGG NAGRTTSGLVSLLTPGAKQNIQLINTNGSWHINSTALNCNESLNTGWLAGLFYQHKFNSSGCPERLASCRRLTDFDQG WGPISYANGSGPDQRPYCWHYPPKPCGIVPAKSVCGPVYCFTPSPVVVGTTDRSGAPTYSWGANDTDVFVLNNTRPPL GNWFGCTWMNSTGFTKVCGAPPCVIGGAGNNTLHCPTDCFRKHPEATYSRCGSGPWITPRCLVDYPYRLWHYPCTINY TIFKVRMYVGGVEHRLEAACNWTRGERCDLEDRDRSELSPLLLSTTQWQVLPCSFTTLPALSTGLIHLHQNIVDVQYL YGVGSSIASWAIKWEYVVLLFLLLADARVCSCLWMMLLISQAEAALENLVILNAASLAGTHGLVSFLVFFCFAWYLKG RWVPGAVYALYGMWPLLLLLLLALPQRAYALDTEVAASCGGVVLVGLMALTLSPYYKRYISWCLWWLQYFLTRVEAQLH VWVPPLNVRGGRDAVILLMCVVHPTLVFDITKLLLAVFGPLWILQASLLKVPYFVRVQGLLRICALARKMIGGHYVQM AIIKLGALTGTYVYNHLTPLRDWAHNGLRDLAVAVEPVVFSQMETKLITWGADTAACGDIINGLPVSARRGREILLGP ADGMVSKGWRLLAPITAYAQQTRGLLGCIITSLTGRDKNQVEGEVQIVSTAAQTFLATCINGVCWTVYHGAGTRTIAS PKGPVIQMYTNVDQDLVGWPAPQGSRSLTPCTCGSSDLYLVTRHADVIPVRRRGDSRGSLLSPRPISYLKGSSGGPLL CPAGHAVGIFRAAVCTRGVAKAVDFIPVENLETTMRSPVFTDNSSPPAVPQSFQVAHLHAPTGSGKSTKVPAAYAAQG YKVLVLNPSVAATLGFGAYMSKAHGIDPNIRTGVRTITTGSPITYSTYGKFLADGGCSGGAYDIIICDECHSTDATSI LGIGTVLDQAETAGARLVVLATATPPGSVTVPHPNIEEVALSTTGEIPFYGKAIPLEVIKGGRHLIFCHSKKKCDELA AKLVALGINAVAYYRGLDVSVIPTSGDVVVVATDALMTGYTGDFDSVIDCNTCVTQTVDFSLDPTFTIETTTLPQDAV SRTQRRGRTGRGKPGIYRFVAPGERPSGMFDSSVLCECYDAGCAWYELTPAETTVRLRAYMNTPGLPVCQDHLEFWEG VFTGLTHIDAHFLSQTKQSGENFPYLVAYQATVCARAQAPPPSWDQMWKCLIRLKPTLHGPTPLLYRLGAVQNEVTLT HPVTKYIMTCMSADLEVVTSTWVLVGGVLAALAAYCLSTGCVVIVGRIVLSGKPAIIPDREVLYREFDEMEECSQHLP YIEQGMMLAEQFKQKALGLLQTASRQAEVIAPAVQTNWQKLEVFWAKHMWNFISGIQYLAGLSTLPGNPAIASLMAFT AAVTSPLTTSQTLLFNILGGWVAAQLAAPGAATAFVGAGLAGAAIGSVGLGKVLVDILAGYGAGVAGALVAFKIMSGE VPSTEDLVNLLPAILSPGALVVGVVCAAILRRHVGPGEGAVQWMNRLIAFASRGNHVSPTHYVPESDAAARVTAILSS LTVTQLLRRLHQWISSECTTPCSGSWLRDIWDWICEVLSDFKTWLKAKLMPQLPGIPFVSCQRGYKGVWRGDGIMHTR CHCGAEITGHVKNGTMRIVGPRTCRNMWSGTFPINAYTTGPCTPLPAPNYTFALWRVSAEEYVEIRRVGDFHYVTGMT TDNLKCPCQVPSPEFFTELDGVRLHRFAPPCKPLLREEVSFRVGLHEYPVGSQLPCEPEPDVAVLTSMLTDPSHITAE AAGRRLARGSPPSMASSSASQLSAPSLKATCTANHDSPDAELIEANLLWRQEMGGNITRVESENKVVILDSFDPLVAE EDEREISVPAEILRKSRRFAQALPVWARPDYNPPLVETWKKPDYEPPVVHGCPLPPPRSPPVPPPRKKRTVVLTESTL STALAELATKSFGSSSTSGITGDNTTTSSEPAPSGCPPDSDAESYSSMPPLEGEPGDPDLSDGSWSTVSSEAGTEDVV CCSMSYSWTGALVTPCAAEEQKLPINALSNSLLRHHNLVYSTTSRSACQRQKKVTFDRLQVLDSHYQDVLKEVKAAAS KVKANLLSVEEACSLTPPHSAKSKFGYGAKDVRCHARKAVAHINSVWKDLLEDSVTPIDTTIMAKNEVFCVQPEKGGR KPARLIVFPDLGVRVCEKMALYDVVSKLPLAVMGSSYGFQYSPGQRVEFLVQAWKSKKTPMGFSYDTRCFDSTVTESD  ${\tt IRTEEAIYQCCDLDPQARVAIKSLTERLYVGGPLTNSRGENCGYRRCRASGVLTTSCGNTLTCYIKARAACRAAGLQD}$ CTMLVCGDDLVVICESAGVQEDAASLRAFTEAMTRYSAPPGDPPQPEYDLELITSCSSNVSVAHDGAGKRVYYLTRDP TTPLARAAWETARHTPVNSWLGNIIMFAPTLWARMILMTHFFSVLIARDQLEQALDCEIYGACYSIEPLDLPPIIQRL HGLSAFSLHSYSPGEINRVAACLRKLGVPPLRAWRHRARSVRARLLARGGRAAICGKYLFNWAVRTKLKLTPIAAAGR LDLSGWFTAGYSGGDIYHSVSHARPRWFWFCLLLLAAGVGIYLLPNR

Scramble - Output File Scramble version : 0.1 beta, 08/02/1999 Num. genes Num. segments : 201 Segment length : 30 Segment overlap Segments in original order: Gene : HepCla Segment# : 1 Offset 1st Codon : 1 S T N P K P Q R K T K R N T N R R P Q D V K F P G G G GCCGCTATGTCCACCAATCCCAAACCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGGAGGCGGA

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Gene : HepCla Segment# : 2 Offset : 16 1st Codon : 1

N T N R R P Q D V K F P G G G Q I V G G V Y L L P R R G P R AACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGA

Gene : HepCla Segment# : 3 Offset : 31 1st Codon : 1

1st Codon : 1
Q I V G G V Y L L P R R G P R L G V R A T R K T S E R S Q P
CAGATTETGGGAGGCGTCTACCTCCTGCCTAGGAGAGGGCCCTAGGCTCAGGCTACCAGAAAGACAAGCGAAAGGTCCCAGCCT

Gene : HepCla
Segment# : 4
Offset : 46
1st Codon : 1

L G V R A T R K T S E R S Q P R G R R Q P I P K A R R P E G CTGGGAGTGAGAGCCCACAGGAAAACCTCCGAGAGGAAGCCCAGAGGCAGAGGCAACCCAGAGGCAACCCAAAGCCAAAGCCAGAAGGCCTGAGGGA

Gene : HepCla
Segment# : 5
Offset : 61
1st Codon : 1

R G R R Q P I P K A R R P E G R T W A Q P G Y P W P L Y G N AGGGGAAGGAGACCCTATCCCTAAGGCTAGGAGACCCGAAGGCAGACCCGGATACCCTTGGCCTCTGTATGGCAAT

Gene : HepCla Segment# : 6 Offset : 76 1st Codon : 1

R T W A Q P G Y P W P L Y G N E G C G W A G W L L S P R G S AGGACATGGCTCAGCCTGGCCCCTCTACGGAAACGAAGGCTGGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCC

Gene : HepCla Segment# : 7 Offset : 91 1st Codon : 1

E G C G W A G W L L S P R G S R P S W G P T D P R R S R N GAGGGATGGGGTGGCTGGCTGGCTCAGCCCTAGGGGAAGCAGACCCTCCTGGGGAACCCACAGACCCTAGGAGAAGGTCCAGGAAT

Gene : HepCla
Segment# : 8
Offset : 106

R P S W G P T D P R R R S R N L G K V I D T L T C G F A D L AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACACTGACATGCGGATTCGCTGACCTC

Gene : HepCla Segment# : 9 Offset : 121 1st Codon : 1

Gene : HepCla Segment# : 10 Offset : 136 1st Codon : 1

M G Y I P L V G A P L G G A A R A L A H G V R V L E D G V N ATGGGATACATTCCCTCGTGGGAGGCCCTCTGGGAGGGCCCTCGCCATGGCGTCAGGGTCATGGAGACACGGAGTGAAT

Gene : HepCla Segment# : 11 Offset : 151 1st Codon : 1

RALAHGVRVLEDGVNYATGNLPGCSFSIFLAGGGCTCTGGCTCACGGAGGGAGGCTCTGGCTCACGGAGTGAGAGTGCTCGAGGATGGCGTCAACTATGCCACAGGCAATCTGCCTGGCTGAGCTTTAGCATTTTCCTC

Gene : HepCla Segment# : 12 Offset : 166

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```
1st Codon : 1
Y A T G N L P G C S F S I F L L A L L S C L T V P A S A Y Q .
TACGCTACCGGAAACCTCCCCGGATGCTCCTTCTCCATCTTTCTGCTCGCCCTCCTGTCCTGCCTCACCGTCCCCGCTAGCGCTTACCAA
Gene
        : HepCla
Segment# : 13
        : 181
Offset
1st Codon : 1
LALLSCLT V P A S A Y Q V R N S T G L Y H V T N D C P
CTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCT
Gene
        : HepCla
Segment# : 14
Offset
       : 196
1st Codon : 1
V R N S T G L Y H V T N D C P N S S I V Y E A A D A I L H T
GTGAGAAACTCCACCGGACTGTATCACGTCACCAATGACTGTCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACA
        : HepCla
Gene
Segment# : 15
        : 211
Offset
1st Codon : 1
N S S I V Y E A A D A I L H T P G C V P C V R E G N A S R C
AACTCCAGCATTGTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGT
Gene
        : HepCla
Segment# : 16
       : 226
Offset
1st Codon: 1
PGCVPCVREGNASRCWVAMTPTVATRDGKL
CCCGGATGCGTCCCCTGTGTGAGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACAGTGGCTACCAGAGACGGAAAGCTC
Gene
        : HepCla
Segment# : 17
Offset
        : 241
: HepCla
Gene
Segment# : 18
Offset
1st Codon : 1
PATQLRRHIDLLVGSATLCSALYVGD LCGS
CCCGCTACCCAACTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTGTGGCTCC
        : HepCla
Segment# : 19
Offset
        : 271
1st Codon: 1
ATLCSALYVGDLCGSVFLVGQLFTFSPRRH
{\tt GCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGCGGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCAT}
Gene
        : HepCla
Segment# : 20
Offset
       : 286
1st Codon : 1
V F L V G Q L F T F S P R R H W T T Q G C N C S I Y P G H I
GTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTATCCCCGGACACATT
        : HepCla
Gene
Segment# : 21
        : 301
Offset
1st Codon: 1
W T T Q G C N C S I Y P G H I T G H R M A W D M M N W S P
TGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCACAGGCCATAGGATGGCCTGGGACATGATGATGAACTGGAGCCCT
        : HepCla
Gene
       : 22
Segment#
        : 316
Offset
T G H R M A W D M M M N W S P T A A L V M A Q L L R I P Q A
ACCGGACACAGAATGGCTTGGGATATGATGATGAATTGGTCCCCCACAGCCGCTCTGGTCATGGCTCAGCTCCTGAGAATCCCTCAGGCT
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Gene : HepCla Segment# : 23 Offset : 331 1st Codon : 1 T A A L V M A Q L L R I P Q A I L D M I A G A H W G V L A G ACCGCTGCCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAGTGCTCGCCGGA : HepCla Segment# : 24 Offset : 346 1st Codon : 1 I L D M I A G A H W G V L A G I A Y F S M V G N W A K V L V Gene : HepCla Segment# : 25 Offset : 361 1st Codon : 1 I A Y F S M V G N W A K V L V V L L L F A G V D A E T H V T Gene : HepCla Segment# : 26 : 376 Offset 1st Codon : 1 V L L F A G V D A E T H V T G G N A G R T T S G L V S L L GTGCTCCTGCTCTTCGCTGGCGTCGACGCTGAGACACACGTCACCGGAGGCAATGCCGGAAGGACAACCTCCGGCCTCGTGTCCCTGCTC Gene : HepCla Segment# : 27 Offset 1st Codon : 1 G G N A G R T T S G L V S L L T P G A K Q N I Q L I N T N G GGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGGA : HepCla Segment# : 28 : 406 1st Codon : 1 T P G A K Q N I Q L I N T N G S W H I N S T A L N C N E S L ACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCAATGGCTCCTGGCATATCAATAGCACAGCCCTCAACTGTAACGAAAGCCTC Gene : HepCla Segment# : 29 : 421 Offset 1st Codon : 1 S W H I N S T A L N C N E S L N T G W L A G L F Y Q H K F N AGCTGGCACATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAATTCAA: HepCla Gene Segment# : 30 Offset : 436 1st Codon : 1 N T G W L A G L F Y Q H K F N S S G C P E R L A S C R R L T AACACAGGCTGGCTGGCTGGCCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGTAGGAGACTGACA : HepCla Segment# : 31 Offset : 451 S S G C P E R L A S C R R L T D F D Q G W G P I S Y A N G S AGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGGATGGGGACCCATTAGCTATGCCAATGGCTCCGene : HepCla Segment# : 32 Offset : 466 1st Codon : 1 D F D O G W G P I S Y A N G S G P D O R P Y C W H Y P P K P GACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCGGACCCGATCAGGACCCTATTGCTGGCACTATCCCCCTAAGCCT Gene : HepCla Segment# : 33

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Offset : 481 1st Codon : 1 G P D Q R P Y C W H Y P P K P C G I V P A K S V C G P V Y C : HepCla Segment# : 34 Offset : 496 1st Codon: 1
C G I V P A K S V C G P V Y C F T P S P V V V G T T D R S G Gene : HepCla Segment# : 35 : 511 Offset 1st Codon: 1
FTPSPVVVGTTDRSGAPTYSWGANDTDVFV TTCACACCCTCCCCGTCGTGGTCGGCACAACCGATAGGTCCGGCGCTCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTC : HepCla Gene Segment# : 36 Offset : 526 1st Codon: 1
APTYSWGANDTDVFVLNNTRPPLGNWFGCT GCCCCTACCTATAGCTGGGGCGCTAACGATACCGATGTGTTTGTGCTCAACAATACCAGACCCCTCTGGGAAACTGGTTCGGATGCACA Gene : НерС1а Segment# : 37 Offset 1st Codon : 1 LNNTRPPLGNWFGCTWMNSTGFTKVCGAPP CTGAATAACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCT Gene : HepCla Segment# : 38 Offset : 556 1st Codon : 1 W M N S T G F T K V C G A P P C V I G G A G N N T L H C P T : HepCla Segment# : 39 Offset C V I G G A G N N T L H C P T D C F R K H P E A T Y S R C G TGCGTCATCGGAGGCGCTGGCAATAACACACTGCATTGCCCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGA Gene : HepCla Segment# : 40 Offset : 586 

 1st Codon: 1

 D C F R K H P E A T Y S R C G S G P W I T P R C L V D Y P Y

 GACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT

 Gene : HepCla Segment# : 41 Offset : 601 1st Codon : 1 S G P W I T P R C L V D Y P Y R L W H Y P C T I N Y T I F K AGCGGACCCTGGATCACACCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTATACCATTTTCAAA : HepCla Gene Segment# : 42 Offset : 616 1st Codon : 1 R L W H Y P C T I N Y T I F K V R M Y V G G V E H R L E A A Gene : HepCla Segment# Offset : 631 1st Codon : 1 V R M Y V G G V E H R L E A A C N W T R G E R C D L E D R D

#### 115/216

```
GTGAGAATGTATGTGGGAGGCGTCGAGCATAGGCTCGAGGCTGCCTGTAACTGGACCAGAGGCGAAAGGTGTGACCTCGAGGATAGGGAT
```

Gene : HepCla
Segment# : 44
Offset : 646
lst Codon : 1
C N W T R G E R C I

Gene : HepCla Segment# : 45 Offset : 661 1st Codon : 1

R S E L S P L L S T T Q W Q V L P C S F T T L P A L S T G AGGTCCGAGCTCAGCCTCTGCTCCACCACAGTGGCAGGTCCTGCCTTGCTCCTTCACAACCCTCCCCGCTCTGCCACCAGGA

Gene : HepCla Segment# : 46 Offset : 676 1st Codon : 1

Gene : HepCla Segment# : 47 Offset : 691 lst Codon : 1

1st Codon: 1
L I H L H Q N I V D V Q Y L Y G V G S S I A S W A I K W E Y
CTGATTCACCTCCACCAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTAT

Gene : HepCla Segment# : 48 Offset : 706 1st Codon : 1

1st Codon : 1 G V G S S 1  $^{\prime}$ A S W A I K W E Y V V L L F L L A D A R V C S GCGTCGGCTCCAGCATTGCCTCCTGGGCTATCAAATGGGAATACGTCGTGCTCCTGGTTCTCTGCTCCTGGCTGACGCTAGGGTCTGCTCC

Gene : HepCla Segment# : 49 Offset : 721 1st Codon : 1

V V L L F L L A D A R V C S C L W M M L L I S Q A E A A L GTGGTCCTGCTCTCCTCGCCGATGCCAGAGTGTTAGCTGTTGTGGATGATGCTGCTCATCTCCCAGGCTGAGGCTGCCCTC

Gene : HepCla Segment# : 50 Offset : 736 1st Codon : 1

Gene : HepCla Segment# : 51 Offset : 751 1st Codon : 1

E N L V I L N A A S L A G T H G L V S F L V F F C F A W Y L GAGAATCTGGTCATCCTCAACGCTGCCTCCCTGGCTGGCACACGGACTGGTCAGCTTTCTGGTCTTCTTTTGCTTTGCCTGGTACCTC

Gene : HepCla Segment# : 52 Offset : 766 lst Codon : 1

G L V S F L V F F C F A W Y L K G R W V P G A V Y A L Y G M GGCCTCGTGTCCTTCGTGTTTTTCGCTTGGTATCTGAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATG

Gene : HepCla Segment# : 53 Offset : 781 1st Codon : 1

K G R W V P G A V Y A L Y G M W P L L L L L A L P Q R A Y AAGGGAAGGTGGGTGCTGGGGTGTGTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTGCTCCTGGCTCTGCCTCAGAGAGCCCTAT

Gene : HepCla

# 116/216

```
Offset
        : 796
1st Codon : 1
 W P L L L L L L L P Q R A Y A L D T E V A A S C G G V V L
TGGCCTCTGCTCCTGCTCCTGCTCCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGGCTGCCTCCTGCGGAGGCGTCGTGCTC
Gene
         : HepCla
Segment# : 55
Offset
        : 811
1st Codon: 1
A L D T E V A A S C G G V V L V G L M A L T L S P Y Y K R Y
GCCCTCGACACAGAGGTCGCCGCTAGCTGTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACACTGTCCCCCTATTACAAAAGGTAT
         : HepCla
Gene
Segment#
        : 56
        : 826
Offset
1st Codon : 1  V \ G \ L \ M \ A \ L \ T \ L \ S \ P \ Y \ Y \ K \ R \ Y \ I \ S \ W \ C \ L \ W \ W \ L \ Q \ Y \ F \ L \ T \ R \ V 
{\tt GTGGGACTGATGGCCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGCCTCTGGTGGCTGCAATACTTTCTGACAAGGGTC}
         : HepCla
Segment# : 57
Offset
        : 841
1st Codon : 1
I S W C L W W L Q Y F L T R V E A Q L H V W V P P L N V R G
ATCTCCTGGTGTCTGTGGTGGCTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGTGGGTGCCTCCCCTCAACGTCAGGGGA
         : HepCla
        : 58
Segment#
        : 856
1st Codon : 1
E A Q L H V W V P P L N V R G G R D A V I L L M C V V H P T
GAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGGGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGTGCATCCCACA
Gene
         : HepCla
Segment# : 59
Offset
        : 871
1st Codon : 1
G R D A V I L L M C V V H P T L V F D I T K L L A V F G P
GGCAGAGACGCTGTGATTCTGCTCATGTGTGTGGTCCACCCTACCCTGTGTTTGACATTACCAAACTGCTCCTGGCTGTGTTTGGCCCT
        : HepCla
Gene
Segment# : 60
L V F D I T K L L A V F G P L W I L Q A S L L K V P Y F V
\tt CTGGTCTTCGATATCACAAAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCTGCTCAAGGTCCCTATTTCGTC
Gene
        : HepCla
Segment# : 61
Offset
        : 901
1st Codon: 1
LWILOASLLKVPYFVRVQGLLRICALARKM
CTGTGGATCCTCCAGGCTAGCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATG
Gene
        : HepCla
Segment# : 62
        : 916
Offset
1st Codon : 1
RVQGLLRICALARKMIGGHYVQMAIIKLGA
AGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCT
        : HepCla
Gene
Segment# : 63
Offset
I G G H Y V Q M A I I K L G A L T G T Y V Y N H L T P L R D
ATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGAT
Segment#
        : 946
```

Figure 26 (Cont)

PCT/AU01/00622 WO 01/090197

## 117/216

LTGTYVYNHLTPLRDWAHNGLRDLAVAVEP : HepCla Segment# : 65 Offset : 961 1st Codon : 1 WAHNGLRDLAVAVEPVVFSQMETKLITWGA : KepCla Segment# : 66 Offset : 976 1st Codon : 1 V V F S Q M E T K L I T W G A D T A A C G D I I N G L P V S  $\tt GTGGTCTTCTCCCAGATGGAGACAAAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTGGCGATATCATTAACGGACTGCCTGTGTCC$ Gene : HepCla Segment# : 67 : 991 Offset 1st Codon : 1 : HepCla Gene Segment# : 68 : 1006 Offset 1st Codon : 1 A R R G R E I L L G P A D G M V S K G W R L L A P I T A Y  ${\tt GCCAGAAGGGGAAGGGAAATCCTCCTGGGACCGCTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCCATTACCGCTTACGCT}$ : HepCla Gene Segment# : 69 : 1021 1st Codon: 1

V S K G W R L L A P I T A Y A Q Q T R G L L G C I I T S L T
GTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACAGCCTATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACA : HepCla Gene Segment# : 70 Offset : 1036 1st Codon: 1 QQTRGLLGCIITSLTGRDKNQVEGEVQIVS CAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAGGTCGAGGGAGAGGTCCAGATTGTGTCC : HepCla Segment# : 71 Offset 1st Codon : 1 G R D K N Q V E G E V Q I V S T A A Q T F L A T C I N G V C  ${\tt GGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGT}$ : HepCla Segment# : 72 Offset : 1066 T A A Q T F L A T C I N G V C W T V Y H G A G T R T I A S P ACCGCTGCCCAAACCTTTCTGGCTACCTGTATCATGGCGTTGCTGGACCGTCTACCATGGCGCTGGCACAAGGACAATCGCTAGCCCT : HepCla Gene Segment# : 73 Offset : 1081 1st Codon : 1 W T V Y H G A G T R T I A S P K G P V I Q M Y T N V D Q D L TGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGACCAAGACCTC Gene : HepCla Segment# : 74

Figure 26 (Cont)

1st Codon : 1 K G P V I Q M Y T N V D Q D L V G W P A P Q G S R S L T P CAAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCGGCTGGCCCGCTCCCCAAGGCTCCAGGTCCCTGACACCCTGT

: 1096

Offset

WO 01/090197

# 118/216

Gene : HepCla Segment# : 75 Offset : 1111 1st Codon : 1 V G W P A P GTGGGATGGCCTGCCCCT

Gene : HepCla Segment# : 76 Offset : 1126 1st Codon : 1

T C G S S D L Y L V T R H A D V I P V R R R G D S R G S L L ACCTGTGGCTCCAGCGATCTGTATCTGGTCACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGAGGGCGATAGCAGAGGCTCCCTGCTC

Gene : HepCla Segment# : 77 Offset : 1141 1st Codon : 1

18t Codon: 1
V I P V R R R G D S R G S L L S P R P I S Y L K G S S G G P
GTGATTCCCGTCAGGAGAGGGGAGACTCCAGGGGAAGCCTCCTGTCCCCCAGACCCATTAGCTATCTGAAAGGCTCCAGCGGAGGCCCT

Gene : HepCla Segment# : 78 Offset : 1156 1st Codon : 1

Gene : HepCla Segment# : 79 Offset : 1171 1st Codon : 1

Gene : HepCla Segment# : 80 Offset : 1186 1st Codon : 1

1st Codon: 1 V C T R G V A K A V D F I P V E N L E T T M R S P V F T D N GTGTGTACCAGAGGCGTCGCCAAAGCCGTCGACTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT

Gene : HepCla Segment# : 81 Offset : 1201 1st Codon : 1

ENLETTMRSPVFTDNSSPPAVPQSFQVAHL GAGAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCGGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTC

Gene : HepCla Segment# : 82 Offset : 1216

Gene : HepCla Segment# : 83 Offset : 1231 1st Codon : 1

Gene : HepCla Segment# : 84 Offset : 1246 1st Codon : 1

Y A A Q G Y K V L V L N P S V A A T L G F G A Y M S K A H G TACGCTGCCCAAGGCTATAAGGTCCTGAATCCCTCCGTGGCTGCCACACTGGATCCGAGGCCTATATGTCCAAGGCTCACGGA

Gene : HepCla Segment# : 85 Offset : 1261

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```
1st Codon : 1
A A T L G F G A Y M S K A H G I D P N I R T G V R T I T T G GCCGCTACCCTCGGCTTTGGCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGA
        : HepCla
Segment# : 86
Offset : 1276
Offset
1st Codon : 1
 ATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTCTGGCTGACGGA
        : HepCla
Gene
Segment# : 87
        : 1291
Offset
1st Codon: 1
SPITYSTYGKFLADGGCSGGAYDIICDEC
AGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGT
        : HepCla
Segment# : 88
        : 1306
Offset
1st Codon : 1
G C S G G A Y D I I I C D E C H S T D A T S I L G I G T V L
: HepCla
Segment# : 89
H S T D A T S I L G I G T V L D Q A E T A G A R L V V L A T
CACTCCACCGATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTCGCCACA
Gene
        : HepCla
Segment# : 90
        : 1336~
Offset
1st Codon : 1
D Q A E T A G A R L V V L A T A T P P G S V T V P H P N I E
GACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCCTGGCTACCGCTACCCCTCCCGGAAGCGTCACCGTCCCCCATCCCAATATCGAA
        : HepCla
Gene
Segment# : 91
        : 1351
A T P P G S V T V P H P N I E E V A L S T T G E I P F Y G K
GCCACACCCCTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAA
        : HepCla
Segment# : 92
Offset
        : 1366
1st Codon : 1
EVALSTTGEIPFYGKAIPLEVIKGGRHLIF
GAGGTCGCCCTCAGCACACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTT
Gene : 25
Segment# : 93
        : HepCla
1st Codon: 1
A I P L E V I K G G R H L I F C H S K K K C D E L A A K L V
GCCATTCCCCTCGAGGTCATCAAAGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGCCAAACTGGTC
        : HepCla
Gene
Segment# : 94
Offset
1st Codon : 1
C H S K K K C D E L A A K L V A L G I N A V A Y Y R G L D V
TGCCATAGCAAAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTC
        : HepCla
Gene
Segment# : 95
Offset
1st Codon : 1
A L G I N A V A Y Y R G L D V S V I P T S G D V V V V A T D
GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGATGTCCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGAT
```

# 120/216

```
: HepCla
Segment#
        : 96
Offset
        : 1426
1st Codon: 1
S V I P T S G D V V V A T D A L M T G Y T G D F D S V I D
AGCGTCATCCCTACCTCCGGCGATGTGGTCGTGGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGAT
Gene
        : HepCla
        : 97
Segment#
Offset
        : 1441
1st Codon: 1
A L M T G Y T G D F D S V I D C N T C V T Q T V D F S L D P
GCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACCGTCGACTTTAGCCTCGACCCT
Gene
        : HepCla
Segment#
       : 98
Offset
        : 1456
1st Codon: 1
C N T C V T Q T V D F S L D P T F T I E T T T L P Q D A V S
TGCAATACCTGTGTGACACAGACAGTGGATTTCTCCCTGGATCCCACATTCACAATCGAAACCACAACCCTCCCCCAAGACGCTGTGTCC
        : HepCla
Gene
Segment# : 99
Offset
1st Codon : 1
T F T I E T T L P Q D A V S R T Q R R G R T G R G K P G I
ACCTTTACCATTGAGACAACCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGGGGAAACCGGAAGGGGGAAAGCCTGGCATT
        : HepCla
Segment#
       : 100
Offset
        : 1486
1st Codon: 1
RTQRRGRTGRGKPGIYRFVAPGERPSGMFD
: HepCla
Gene
Segment# : 101
Offset
       : 1501
1st Codon : 1
Y R F V A P G E R P S G M F D S S V L C E C Y D A G C A W Y
TACAGATTCGTCGCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTGTGAGTGTTACGATGCCGGATGCGCTTGGTAT
Segment#
       : 102
Offset
        : 1516
1st Codon : 1
S S V L C E C Y D A G C A W Y E L T P A E T T V R L R A Y M
AGCTCCGTGCTCTGCGAATGCTATGACGCTGGCTGTGCCTGGTACGAACTGACACCCGCTGAGACAACCGTCAGGCTCAGGGCTTACATG
Gene
        : HepCla
Segment# : 103
Offset
       : 1531
1st Codon : 1
       PAETTVRLRAYMNTPGLPVCQDHLEFW
GAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCATCTGGAATTCTGG
        : HepCla
Gene
Segment# : 104
Offset
       : 1546
1st Codon : 1
N T P G L P V C Q D H L E F W E G V F T G L T H I D A H F L
AACACACCGGACTGCCTGTGTCAGGATCACCTCGAGTTTTGGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTC
        : HepCla
       : 105
Segment#
       : 1561
Offset
EGVFTGLTHIDAHFLSQTKQSGENFPYLVA
GAGGGAGTGTTTACCGGACTGACACACACTGACGCTCACTTTCTGTCCCAGACAAAGCGAAAAGCGGAGAGAATTTCCCTTACCTCGTGGCT
Gene
        : HepCla
Segment# : 106
```

### 121/216

Offset : 1576 1st Codon : 1 S Q T K Q S G E N F P Y L V A Y Q A T V C A R A Q A P P P S : HepCla Segment# : 107 : 1591 1st Codon : 1 YQATVCARAQAPPPSWDQMWKCLIRLKPTL TACCAAGCCACAGTGTGTGCCAGAGCCCAAGCCCCTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTC : HepCla Segment# : 108 : 1606 W D Q M W K C L I R L K P T L H G P T P L L Y R L G A V Q N TGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTCTACAGACTGGGAGCCGTCCAGAAT : HepCla Segment# : 109 Offset : 1621 1st Codon: 1

H G P T P L L Y R L G A V Q N E V T L T H P V T K Y I M T C CACGGACCCACACCCCTCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACTGACACACCCTGTGACAAAGTATATCATGACCTGT Gene : HepCla Segment# : 110 Offset : 1636 1st Codon: 1
EVTLTHPVTKYIMTCMSADLEVVTSTWVLV : HepCla Segment# : 111 > Offset : 1651 1st Codon : 1 M S A D L E V V T S T W V L V G G V L A A L A A Y C L S T G ATGTCCGCCGATCTGGAAGTGGTCACCTCCACCTGGGTGCTCGTGGGAGGCGTCCTGGCTGCCCTCGCCGCTTACTGTCCACCGGA : HepCla Segment# : 112 Offset : 1666 1st Codon : 1 G G V L A A L A A Y C L S T G C V V I V G R I V L S G K P A GGGGAGTGCTCGCCGCTCTGGCTGCCTATTGCCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCT Gene : HepCla Segment# : 113 : 1681 Offset 1st Codon : 1 CVVIVGRIVLSGKPAIIPDREVLYREFDEM TGCGTCGTGATTGTGGGAAGGATTGTGCTCAGCGGAAAGCCTGCCATTATCCCTGACAGAGAGGTCCTGTATAGGGAATTCGATGAGATG : HepCla Segment# : 114 Offset : 1696 1st Codon : 1  $\begin{smallmatrix}\mathbf{I}&\mathbf{I}&\mathbf{P}&\mathbf{D}&\mathbf{R}&\mathbf{E}&\mathbf{V}&\mathbf{L}&\mathbf{Y}&\mathbf{R}&\mathbf{E}&\mathbf{F}&\mathbf{D}&\mathbf{E}&\mathbf{M}&\mathbf{E}&\mathbf{E}&\mathbf{C}&\mathbf{S}&\mathbf{Q}&\mathbf{H}&\mathbf{L}&\mathbf{P}&\mathbf{Y}&\mathbf{I}&\mathbf{E}&\mathbf{Q}&\mathbf{G}&\mathbf{M}&\mathbf{M}\end{smallmatrix}$ ATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATG Gene : HepCla Segment# : 115 : 1711 1st Codon: 1
E E C S Q H L P Y I E Q G M M L A E Q F K Q K A L G L L Q T GAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACA : HepCla Segment# : 116 Offset : 1726 1st Codon : 1 LAEQFKQKALGLLQTASRQAEVIAPAVQTN

#### 122/216

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\tt CTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGGTCATCGCTCCCGCTGTGCAAACCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCAATCAATCCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCA
```

```
: HepCla
Gene
Segment#
       : 117
Offset
       : 1741
1st Codon : 1
A S R Q A E V I A P A V Q T N W Q K L E V F W A K H M W N F
{\tt GCCTCCAGGCAAGCCGAAGTGATTGCCCCTGCCGTCCAGACAAACTGGCAGAAACTGGAAGTGTTTTGGGCTAAGCATATGTGGAACTTT}
        : HepCla
Gene
Segment# : 118
Offset
       : 1756
1st Codon : 1
W Q K L E V F W A K H M W N F I S G I Q Y L A G L S T L P G
TGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCAATACCTCGCCGGACTGTCCACCCTCCCCGGA
        : HepCla
Gene
Segment#
       : 119
Offset
       : 1771
1st Codon : 1
I S G I Q Y L A G L S T L P G N P A I A S L M A F T A A V T
ATCTCCGGCATTCAGTATCTGGCTGGCCTCAGCACACTGCCTGGCAATCCCGCTATCGCTAGCCTCATGGCTTTCACAGCCGCTGTGACA
        : HepCla
Segment# : 120
Offset
       : 1786
1st Codon : 1
N P A I A S L M A F T A A V T S P L T T S Q T L L F N I L G
AACCCTGCCATTGCCTCCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCCTCACCACAAGCCCAAACCCTCCTGTTTAACATTCTGGGA
Gene
        : HepCla
Segment#
       : 121
Offset
       : 1801
1st Codon : 1
S P L T T S Q T L L F N I L G G W V A A Q L A A P G A A T A
AGCCCTCTGACAACCTCCCAGACACTGCTCTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCT
       : HepCla
Gene
Segment# : 122
       : 1816
Offset
1st Codon : 1
           Q L A A P G A A T A F V G A G L A G A A I G S V G
Gene
       : HepCla
Segment# : 123
Offset
       : 1831
1st Codon : 1
F V G A G L A G A A I G S V G L G K V L V D I L A G Y G A G
TTCGTCGGCGCTGGCCTGGCCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCGGA
       : HepCla
Gene
Segment#
       : 124
Offset
       : 1846
1st Codon : 1
L G K V L V D I L A G Y G A G V A G A L V A F K I M S G E V
CTGGGAAAGGTCCTGGTCGACATTCTGGCTGGCTATGGCGCTGGCGTCGCCGGAGCCCTCGTGGCTTTCAAAATCATGAGCGGAGAGGTC
Gene
       : HepCla
Segment# : 125
       : 1861
1st Codon: 1
VAGALVAFKIMSGEVPSTEDLVNLLPAILS
Gene
       : HepCla
Segment# : 126
Offset
       : 1876
1st Codon : 1
P S T E D L V N L L P A I L S P G A L V V G V V C A A I L R
CCCTCCACCGAGACCCTCGTGAATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTGGGGAGTGGTCTGCGCTGCCATTCTGAGA
```

Figure 26 (Cont)

Gene

: HepCla

# 123/216

Segment# : 127 Offset : 1891 1st Codon : 1

Gene : HepCla Segment# : 128 Offset : 1906 1st Codon : 1

RHVGPGEGAVQWMNRLIAFASRGNHVSPTH AGGCATGTGGGACCCGGAGAGGGAGCCGTCCAGTGGATGAATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCTACCCAT

Gene : HepCla Segment# : 129 Offset : 1921 1st Codon : 1

L I A F A S R G N H V S P T H Y V P E S D A A A R V T A I L CTGATTGCCTTCGCGGGGAAACCATGTGTCCCCCACACACTATGTGCCTGAGTCCGACGCTGCGCTAGGGTCACCGCTATCCTC

Gene : HepCla Segment# : 130 Offset : 1936

1st Codon: 1
Y V P E S D A A A R V T A I L S S L T V T Q L L R R L H Q W
TACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCGACTGCTCAGGAGACTGCATCAGTGG

Gene : HepCla Segment# : 131 Offset : 1951 1st Codon : 1

Gene : HepCla : Segment# : 132
Offset : 1966
1st Codon : 1

I S S E C T T P C S G S W L R D I W D W I C E V L S D F K T ATCTCCAGCGAATGCACACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGATCTGTGAGGTCCTGTCCGACTTTAAGACA

Gene : HepCla Segment# : 133 Offset : 1981 1st Codon : 1

D I W D W I C E V L S D F K T W L K A K L M P Q L P G I P F GACATTTGGGATTGCGAAGTGCTCAGCGATTCCAAAACCTGGCTGAAAGCCAAACTGATGCCCCAACTGCCTGGCATTCCCTTT

Gene : HepCla Segment# : 134 Offset : 1996 1st Codon : 1

W L K A K L M P Q L P G I P F V S C Q R G Y K G V W R G D G
TGGCTCAAGGCTAAGGCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGCAGAGAGGCTATAAGGGAGTGTGGAGGGGAACACGA

Gene : HepCla Segment# : 135 Offset : 2011

V S C Q R G Y K G V W R G D G I M H T R C H C G A E I T G H GTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGAAGCCGAAATCACAGGCCAT

Gene : HepCla Segment# : 136 Offset : 2026 1st Codon : 1

Gene : HepCla Segment# : 137 Offset : 2041 1st Codon : 1

# 124/216

V K N G T M R I V G P R T C R N M W S G T F P I N A Y T T G GTGAAAAACGGAACCATGAGGATTGTGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGGA

Gene : HepCla Segment# : 138 Offset : 2056 1st Codon : 1

N M W S G T F P I N A Y T T G P C T P L P A P N Y T F A L W AACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCGGTCCCAATTACACATTCGCTCTGTGG

Gene : HepCla
Segment# : 139
Offset : 2071
Let Codon : 1

1st Codon: 1
PCTPLPAPNYTFALWRVSAEEYVEIRRVGD
CCCTGTACCCCTCTGCCCCCTAACTATACCTTTGCCCTCTGGAGAGTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGAT

Gene : HepCla Segment# : 140 Offset : 2086 1st Codon : 1

R V S A E E Y V E I R R V G D F H Y V T G M T T D N L K C P AGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTATGTGACAGGCATGACCACAGACAATCTGAAATGCCCT

Gene : HepCla Segment# : 141 Offset : 2101 1st Codon : 1

Gene : HepCla Segment# : 142 Offset : 2116 1st Codon : 1

C Q V P S P E F F T E L D G V R L H R F A P P C K P L L R E TGCCAAGTGCCTAGCCCTGAGTTTTTCACAGAGCTCGACGGAGTGAGACTGCATAGGTTTGCCCCTCCTGTAAGCCTCTGCTCAGGGAA

Gene : HepCla Segment# : 143 Offset : 2131 1st Codon : 1

R L H R F A P P C K P L L R E E V S F R V G L H E Y P V G S AGGCTCCACAGATTCGCCTCCCTTGCAAACCCCTCCTGAGAGGGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCGGCTCC

Gene : HepCla Segment# : 144 Offset : 2146 1st Codon : 1

Gene : HepCla Segment# : 145 Offset : 2161 lst Codon : 1

1st Codon : 1
Q L P C E P E P D V A V L T S M L T D P S H I T A E A A G R
CAGCTCCCCTGTGAGCCTGACCTGCCCGTCCTGACAGCAGCCTGCCAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGA

Gene : HepCla Segment# : 146 Offset : 2176 1st Codon : 1

Gene : HepCla Segment# : 147 Offset : 2191 1st Codon : 1

R L A R G S P P S M A S S S A S Q L S A P S L K A T C T A N AGGCTCGCCAGAGGCTCCCCCTAGCATGCATGCCTCCAGCTCCCAGCTCCCTGCAGAGCCACATGCACAGCCAAT

# 125/216

Gene : HepCla Segment# : 148 Offset : 2206 1st Codon : 1

S Q L S A P S L K A T C T A N H D S P D A E L I E A N L L W AGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGATGCCGAACTGATTGAGGCTAACCTCCTGTGG

Gene : HepCla Segment# : 149 Offset : 2221 1st Codon : 1

lst Codon: 1

H D S P D A E L I E A N L L W R Q E M G G N I T R V E S E N
CACGATAGCCCTGACGCTGAGCTCATCGAAGCCAATCTGCTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAAT

Gene : HepCla Segment# : 150 Offset : 2236 1st Codon : 1

R Q E M G G N I T R V E S E N K V V I L D S F D P L V A E E AGGCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAGCGAAACAAGTGGTCATCCTCGATCCTCGATCCTCGTGGCTGAGGAA

Gene : HepCla Segment# : 151 Offset : 2251 1st Codon : 1

Gene : HepCla Segment# : 152 Offset : 2266 1st Codon : 1

1st Codon: 1
DEREISVPAEILRKSRRFAQALPVWARPDY
GACGAAAGGGAAATCTCCGTGCCGAAATCCTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCGTCTGGGCTAGGCCTGACTAT

Gene : HepCia Segment# : 153 Offset : 2281 1st Codon : 1

1st Codon: 1
R R F A Q A L P V W A R P D Y N P P L V E T W K K P D Y E P
AGGAGATTCGCTCAGGCTCTGCCTGTGGGCCAGACCCGATTACAATCCCCCTCTGGTCGAGAAAAAGCCTGACTATGAGCCT

Gene : HepCla Segment# : 154 Offset : 2296 1st Codon : 1

N P P L V E T W K K P D Y E P P V V H G C P L P P P R S P P AACCCTCCCTCGTGGAAACCTGGAAACCCGATTACGAACCCCCTGTGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCCCT

Gene : HepCla Segment# : 155 Offset : 2311 1st Codon : 1

1st Codon: 1
PV V H G C P L P P P R S P P V P P P R K K R T V V L T E S
CCCGTCGTGCATGGCTGTCCCCTCCCCGGAAGCCCTCCCGGTCCCCCCTCCCAGAAGAAAAAGGACAGTGGTCCTGACAGAGTCC

Gene : HepCla Segment# : 156 Offset : 2326 1st Codon : 1

Gene : HepCla Segment# : 157 Offset : 2341 1st Codon : 1

T L S T A L A E L A T K S F G S S S T S G I T G D N T T T S ACCCTCAGCACAGCCCTCGGCGAACTGGCTACCAAAAGCTTTGGCTCCAGCTCCAGCACTCCGGCATTACCGGAGACAATACCACAACCTCC

Gene : HepCla Segment# : 158 Offset : 2356

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1st Codon : 1 S S S T S G I T G D N T T T S S E P A P S G C P P D S D A E AGCTCCAGCACAAGCGGAATCACAGGCGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGCGGATGCCCTCCCGATAGCGATGCCGAA : HepCla Segment# : 159 : 2371 Offset 1st Codon : 1 SEPAPSGCPPDSDAESYSSMPPLEGEPGDP AGCGAACCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGGAGACCCT : HepCla Gene Segment# : 160 : 2386 S Y S S M P P · L E G E P G D P D L S D G S W S T V S S E A G AGCTATAGCTCCATGCCTCCCCTCGAGGGAGAGCCTGGCGATCCCGATCTGTCCGACGGAAGCTGGAGCACAGTGTCCAGCGAAGCCGGA : HepCla Segment# : 161 Offset : 2401 1st Codon : 1 D L S D G S W S T V S S E A G T E D V V C C S M S Y S W GACCTCAGCGATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGA : HepCla Gene Segment# : 162 : 2416 Offset 1st Codon : 1 T E D V V C C S M S Y S W T G A L V T P C A A E E Q K L P I ACCGAAGACGTCGTGTGTTGCTCCATGTCCTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCAAAAGCTCCCCATT : HepCla Gene : 163 Segment# : 2431 ALVTPCAAEEQKLPINALSNSLL'RHHNLVY GCCCTCGTGACACCCTGTGCCGCTGAGGAACAGAAACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCCATAACCTCGTGTAT Gene : HepCla : 164 Segment# : 2446 Offset 1st Codon : 1 N A L S N S L L R H H N L V Y S T T S R S A C Q R Q K K V T : HepCla Gene Segment# : 165 : 2461 STTSRSACQRQKKVTFDRLQVLDSHYQDVL AGCACAACCTCCAGGTCCGCCTGTCAGAGACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTC : HepCla Segment# : 166 Offset : 2476 1st Codon: 1
FDRLQVLDSHYQDVLKEVKAAASKVKANLL TTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAGAGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTC Gene : HepCla Segment# : 167 Offset : 2491 1st Codon : 1 K E V K A A A S K V K A N L L S V E E A C S L T P P H S A K AAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTGCGTGGAAGAGGGCTTGCTCCCTGACACCCCCTCACTCCGCCAAA : HepCla Gene : 168 Segment# : 2506 Offset 1st Codon : 1 S V E E A C S L T P P H S A K S K F G Y G A K D V R C H A R

AGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTCCAAGTTTGGCTATGGCGCTAAGGATGTGAGATGCCATGCCAGA

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Gene : HepCla
Segment# : 169
Offset : 2521
Let Codon : 3

1st Codon: 1
S K F G Y G A K D V R C H A R K A V A H I N S V W K D L L E
AGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCACGCTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAA

Gene : HepCla Segment# : 170 Offset : 2536 1st Codon : 1

K A V A H I N S V W K D L L E D S V T P I D T T I M A K N E AAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTGCTCGAGGATAGCGTCACCCCTATCGATACCACAATCATGGCCAAAAACGAA

Gene : HepCla Segment# : 171 Offset : 2551 1st Codon : 1

D S V T P I D T T I M A K N E V F C V Q P E K G G R K P A R GACTCCGTGACACCCATTGACAACCATTATGGCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGA

Gene : HepCla Segment# : 172 Offset : 2566 lst Codon : 1

1st Codon : 1
V F C V Q P E K G G R K P A R L I V F P D L G V R V C E K M
GTGTTTTGCGTCCAGCCTGAGAAAGGCGGAAGGAAACCCGCTAGGCTCATCGTCTTCCCTGACCTCGGCGTCAGGGTCTGCGAAAAGATG

Gene : HepCla Segment# : 173 Offset : 2581 1st Codon : 1

L I V F P D L G V R V C E K M A L Y D V V S K L P L A V M G CTGATTGTGTTTCCCGATCTGGGAGAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCCTCGCCGTCATGGGA

Gene : HepCla Segment# : 174 Offset : 2596 1st Codon : 1

A L Y D V V S K L P L A V M G S S Y G F Q Y S P G Q R V E F GCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGGCTCCAGCTATGGCTTTCAGTATAGCCCTGGCCAAAGGGTCGAGTTT

Gene : HepCla Segment# : 175 Offset : 2611 1st Codon : 1

Gene : HepCla Segment# : 176 Offset : 2626

Gene : HepCla Segment# : 177 Offset : 2641 1st Codon : 1

Gene : HepCla Segment# : 178 Offset : 2656 1st Codon : 1

R T E E A I Y Q C C D L D P Q A R V A I K S L T E R L Y V G AGGACAGAGGAAGCCATTTACCAATGCTGTGACCCTCAGCCTCAGGCTAGGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGA

Gene : HepCla Segment# : 179

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Offset : 2671 1st Codon : 1 A R V A I K S L T E R L Y V G G P L T N S R G E N C G Y R R GCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACCCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGA : HepCla Segment# : 180 Offset : 2686 1st Codon : 1 G P L T N S R G E N C G Y R R C R A S G V L T T S C G N T L Gene : HepCla Segment# : 181 Offset : 2701 1st Codon : 1 C R A S G V L T T S C G N T L T C Y I K A R A A C R A A G L TGCAGAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTGGCCTC Gene : HepCla Segment# T C Y I K A R A A C R A A G L Q D C T M L V C G D D L V V I ACCTGTTACATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCTGCGGAGACGATCTGGTCGTGATT : HepCla Segment# : 183 Offset : 2731 1st Codon : 1 Q D C T M L V C G D D L V V I C E S A G V Q E D A A S L R A CAGGATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCTCAGGGCT : HepCla Gene Segment# : 184 Offset : 2746 1st Codon : 1 C E S A G V Q E D A A S L R A F T E A M T R Y S A P P G D P TGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGGAGACCCT : HepCla Segment# : 185 Offset : 2761 1st Codon: 1

F T E A M T R Y S A P P G D P P Q P E Y D L E L I T S C S S TTCACAGAGGCTATGACAAGCTATAGCGCTCCCCTGGCGATCCCCTCAGCCTGAGCTTGAGCTCATCACAAGCTGTAGCTCC Gene : HepCla Segment# : 186 Offset : 2776 1st Codon : 1 P Q P E Y D L E L I T S C S S N V S V A H D G A G K R V Y Y CCCCAACCCGAATACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTAT : HepCla Gene : 187 Segment# Offset 1st Codon : 1 N V S V A H D G A G K R V Y Y L T R D P T T P L A R A A W E AACGTCAGCGTCGCCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACACCCCTCGCCAGAGCCCCTTGGGAA Gene : HepCla : 188 Segment# Offset : 2806 1st Codon : 1 L T R D P T T P L A R A A W E T A R H T P V N S W L G N I CTGACAAGGGATCCCACAACCCCTCTGGCTAGGGCTGCCTGGGAGACAGCCAGACACACCCCGTCAACTCCTGGCTCGGCAATATCATT Gene : HepCla Segment# : 189 Offset : 2821

Figure 26 (Cont)

T A R H T P V N S W L G N I I M F A P T L W A R M I L M T H

1st Codon : 1

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ACCGCTAGGCATACCCCTGTGAATAGCTGGCTGGGAAACATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCAT
Segment# : 190
1st Codon : 1
 M F A P T L W A R M I L M T H F F S V L I A R D Q L E Q A L
ATGTTTGCCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGGATCAGCTCGAGCCAAGCCCTC
                : HepCla
Segment# : 191
                : 2851
 FFSVLIARDQLEQALDCEIYGACYSIEPLD
: HepCla
Segment# : 192
               : 2866
Offset
1st Codon : 1
 D C E I Y G A C Y S I E P L D L P P I I Q R L H G L S A F S
GACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCTATCATTCAGAGACTGCATGGCCTCAGCGCTTTCTCC
Gene
                : HepCla
Segment# : 193
Offset
               : 2881
1st Codon : 1
L P P I I Q R L H G L S A F S L H S Y S P G E I N R V A A C
CTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCGGAGAGATTAACAGAGTGGCTGCTGT
                : HepCla
Gene
Segment# : 194
               : 2896
Offset
1st Codon : 1
 L H S Y S P G E I N R V A A C L R K L G V P P L R A W R H R
\tt CTGCATAGCCTATGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGACACAGA
               : HepCla
Segment# : 195
               : 2911
Offset
1st Codon : 1
 L R K L G V P P L R A W R H R A R S V R A R L L A R G G R A
\tt CTGAGAAAGCTCGGCGTCCCCCTCTGAGAGCCTGGAGGCATAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGCGGAAGGGCTTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGCGGAAGGGCTTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGCGGAAGGGCTTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGCGGAAGGGCTTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGGCGGAAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGCGGAAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGCGGAAGGGCGAAGGGCTAGGTCCGTGAGAGGCCAGACTGCTCGCCAGAGGCGGAAGGGCTAGGTCCGTGAGAGGCCAGACTGCTCGCCAGAGGCGGAAGGGCGAAGGGCTAGGTCCGTGAGAGGCCAGACTGCTCGCCAGAGGGCGGAAGGGCGAAGGGCTAGGTCCGTGAGAGGCCAGACTGCTCGCCAGAGGGCGGAAGGGCGAAGGGCGAAGGGCGAAGGGCAGACTGCTCGCCAGAGGCCAGACTGCTCGCCAGAGGGCGGAAGGGCGAAGGGCAGACTGCTCGCCAGAGGGCGGAAGGGCGGAAGGGCAGACTGCTCGCCAGAGGGCGGAAGGGCGGAAGGGCAGACTGCTCGCCAGAGGCCAGACTGCTCGCCAGAGGGCGGAAGGGCGGAAGGGCAGACTGCTCGCCAGAGGCCAGACTGCTCGCCAGAGGCCAGACTGCTCGCCAGAGGCCAGACTGCTCGCCAGAGGCCAGACTGCTCGCAGAGGCCAGACTGCTCGCCAGAGGCCAGACTGCTCGCCAGAGGCCAGACTGCTCGCCAGAGGCCAGACTGCTCGCCAGAGGCCAGACTGCTCGCCAGAGGCCAGACTGCTCGCCAGAGGCCAGACTGCTCAGACTGCTCGCCAGAGGCCAGACTGCTCAGACTCCAGACTGCTCAGACTGCTCAGACTGCTCAGACTGCTCAGACTGCTCAGACTGCTCAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGACTAGA
Gene
                : HepCla
Segment# : 196
               : 2926
Offset
1st Codon : 1
 ARSVRARLLARGGRAAICGKYLFNWAVRTK
GCCAGAAGCGTCAGGGCTAGGCTCCTGGCTAGGGGAGGCAGAGCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAA
                : HepCla
Gene
Segment# : 197
Offset
1st Codon : 1
 A I C G K Y L F N W A V R T K L K L T P I A A A G R L D L S
GCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGATCTGTCC
Gene
                : HepCla
Segment# : 198
              : 2956
 L K L T P I A A G R L D L S G W F T A G Y S G G D I Y H S
: HepCla
Gene
Segment# : 199
Offset
               : 2971
lst Codon: 1
G W F T A G Y S G G D I Y H S V S H A R P R W F W F C L L L
Gene
               : HepCla
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Segment# : 200 Offset : 2986 1st Codon : 1

V S H A R P R W F W F C L L L A A G V G I Y L L P N R A A GTGTCCCACGCTAGGCCTAGGTGTTCTGGTTCTGCTCCTGCTCGCCGCTGGCGTCGGCATTTACCTCCTGCCTAACAGAGCCGCT

: HepCla Segment# : 201 Offset : 3001 1st Codon : 1

LAAGVGIYLLPNRAA CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCC

Segments in scrambled order:

HepCla #77

VIPVRRRGDSRGSLLSPRPISYLKGSSGG GTGATTCCCGTCAGGAGAAGGGGAGACTCCAGGGGAAGCCTCCTGTCCCCCAGACCCATTAGCTATCTGAAAGGCTCCAGCGGAGGCCCT

A R R G R E I L L G P A D G M V S K G W R L L A P I T A Y A GCCAGAAGGGGAAGGGAAATCCTCCTGGGACCCGCTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCTGGCTCCCATTACCGCTTACGCT

RLHRFAPPCKPLLREEVSFRVGLHEYPVGS AGGCTCCACAGATTCGCTCCCCTTGCAAACCCCTCCTGAGAGAGGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCGGCTCC

V V F S Q M E T K L I T W G A D T A A C G D I I N G L P V S GTGGTCTTCTCCCAGATGGAGACAAAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTGGCGATATCATTAACGGACTGCCTGTGTCC

L L C P A G H A V G I F R A A V C T R G V A K A V D F I P V  $\tt CTGCTCTGCCCTGCCGGACACGCTGTGGGAATCTTTAGGGCTGCCGTCTGCACAAGGGGAGTGGCTAAGGCTGTGGATTTCATTCCCGTC$ 

C V V I V G R I V L S G K P A I I P D R E V L Y R E F D E M TGCGTCGTGATTGTGGGAAGGATTGTGCTCAGCGGAAAGCCTGCCATTATCCCTGACAGAGAGGTCCTGTATAGGGAATTCGATGAGATG

HepCla #139
PCTPLPAPNYTFALWRVSAEEYVEIRRVGD CCCTGTACCCCTCTGCCCCTAACTATACCTTTGCCCTCTGGAGAGTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGAT

HepCla #174
A L Y D V V S K L P L A V M G S S Y G F Q Y S P G Q R V E F CCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGGCTCCAGCTATGGCTTTCAGTATAGCCCTGGCCAAAGGGTCGAGTTT

HepCla #57

ISWCLWWLQYFLTRVEAQLHVWVPPLNVRG ATCTCCTGGTGTCTGTGGTGGCTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGTGGGTGCCTCGCCTCAACGTCAGGGGA

ENLVILNAASLAGTHGLVSFLVFFCFAWYL GAGAATCTGGTCATCCTCAACGCTGCCTCCCTGGCTGGCACACACGGACTGGTCAGCTTTCTGGTCTTCTTTTGCTTTGCCTGGTACCTC

PPII Q R L H G L S A F S L H S Y S P G E I N R V A A C CTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCGGAGAGATTAACAGAGTGGCTGCCTGT

N P P L V E T W K K P D Y E P P V V H G C P L P P P R S P P AACCCTCCCTCGTGGAAACCTGGAAGAACCCGATTACGAACCCCCTGTGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCCT

G V G S S I A S W A I K W E Y V V L L F L L L A D A R V C S GGCGTCGGCTCCAGCATTGCCTCCTGGGCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCC

LNNTRPPLGNWFGCTWMNSTGFTKVCGAPP  $\tt CTGAATAACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCT$ 

HepCla #185

F T E A M T R Y S A P P G D P P Q P E Y D L E L I T S C S S

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HepCla #54
W P L L L L L A L P Q R A Y A L D T E V A A S C G G V V L TGGCCTCTGCTCCTGCTCGCCCCTCCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGGCTGCCTCCTGCGGAGGCGTCGTGCTC

Q Q T R G L L G C I I T S L T G R D K N Q V E G E V Q I V S CAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAGGTCGAGGGAGAGGTCCAGATTGTGTCC

HepCla #82

S S P P A V P Q S F Q V A H L H A P T G S G K S T K V P A A 

N T P G L P V C Q D H L E F W E G V F T G L T H I D A H F L AACACCCGGACTGCCTGTGTGTCAGGATCACCTCGAGTTTTGGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTC

HepCla #26
V L L L F A G V D A E T H V T G G N A G R T T S G L V S L L 

EVTLTHPVTKYIMTCMSADLEVVTSTWVLV 

V G L M A L T L S P Y Y K R Y I S W C L W W L Q Y F L T R V GTGGGACTGATGCCCTCACCCTTACTATAAGAGATACATTAGCTGGTGCCTCTGGTGGCTGCAATACTTTCTGACAAGGGTC

AICGKYLFNWAVRTKLKLTPIAAAGRLDLS GCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGATCTGTCC

HepCla #25 ...
I A Y F S M V G N W A K V L V V L L F A G V D A E T H V T ATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTTCTGTTTGCCGGAGTGGATGCCGAAACCCATGTGACA

R L A R G S P P S M A S S S A S Q L S A P S L K A T C T A N 

HepCla #52
G L V S F L V F F C F A W Y L K G R W V P G A V Y A L Y G M
GGCCTCGTGTCCTCCTCGTGTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATG

HepCla #145 Q L P C E P E P D V A V L T S M L T D P S H I T A E A A G R CAGCTCCCCTGTGAGCCTGACCTGACGTCGCCGTCCTGACAAGCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGA

HepCla #171 DSVTPIDTTIMAKNEVFCVQPEKGGRKPAR GACTCCGTGACACCCATTGACACAACCATTATGGCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGA

HepCla #84

Y A A Q G Y K V L V L N P S V A A T L G F G A Y M S K A H G TACGCTGCCCAAGGCTATAAGGTCCTGGTCCTGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGA

HepCla #14

V R N S T G L Y H V T N D C P N S S I V Y E A A D A I L H T 

HepCla #175

S S Y G F Q Y S P G Q R V E F L V Q A W K S K K T P M G F S AGCTCCTACGGATTCCAATACTCCCCCGGACAGAGAGTGGAATTCCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCC

D T A A C G D I I N G L P V S A R R G R E I L L G P A D G M 

S Q L S A P S L K A T C T A N H D S P D A E L I E A N L L W AGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGATGCCGAACTGATTGAGGCTAACCTCCTGTGG

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HepCla #120

N P A I A S L M A F T A A V T S P L T T S Q T L L F N I L G
AACCCTGCCATTGCCTCCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCCTCACCACAGCCCAAACCCTCCTGTTTAACATTCTGGGA

HepCla #176

L V Q A W K S K K T P M G F S Y D T R C F D S T V T E S D I

CTGGTCCAGGCTTGGAAAAGCAAAAGACACCCATGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGACAGAGTCCGACATT

HepCla #152 .

D E R E I S V P A E I L R K S R R F A Q A L P V W A R P D Y GACGAAAGGGAAATCTCCGTGCCTGCCTGAATCCTCAGGAAAGCAGAAGGTTTGCCCAAGCCCTCCCCGTCTGGGCTGACCTAT

M F A P T L W A R M I L M T H F F S V L I A R D Q L E Q A L
ATGITIGCCCTACCCTCGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTC

HEPCIA #96
S V I P T S G D V V V V A T D A L M T G Y T G D F D S V I D
AGCGTCATCCCTACCTCCGGCGATGTGGTCGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGAT

HepCla #94
C H S K K K C D E L A A K L V A L G I N A V A Y Y R G L D V
TGCCATAGCAAAAGAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTC

HepCla #53

K G R W V P G A V Y A L Y G M W P L L L L L A L P Q R A Y
AAGGGAAGGTGGGTGCCTGTGTGTGTCCCTTACGGAATGTGGCCCCTCCTGCTCCTGCTCCTGCTCTGCTCTAGAGAGCCTAT

HepCla #87
S P I T Y S T Y G K F L A D G G C S G G A Y D I I I C D E C
AGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGT

HepCla #196

A R S V R A R L L A R G G R A A I C G K Y L F N W A V R T K
GCCAGAAGCGTCAGGGCTAGGCTCCTGGCTAGGGGAGGCAGAGCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAA

HepCla #170
K A V A H I N S V W K D L L E D S V T P I D T T I M A K N E
AAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTGCTCGAGGATAGCGTCACCCCTATCGATACCACAATCATGGCCAAAAACGAA

HepCla #35

F T P S P V V V G T T D R S G A P T Y S W G A N D T D V F V

TTCACACCCTCCCCGTCGTCGTCGGCACAACCGATAGGTCCGGCGCTCCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTC

HepCla #16

P G C V P C V R E G N A S R C W V A M T P T V A T R D G K L

CCCGGATGCGTCCCCTGTGTGAGAGAGGGAAAGGCTAGCAGATGCTGGGTGGCTATGACACCCCACAGTGGCTACCAGAGACGGAAAGCTC

HepCla #183
Q D C T M L V C G D D L V V I C E S A G V Q E D A A S L R A
CAGGATTGCACAATGCTGGTGTGGGGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCTCAGGGCT

HepCla #125

V A G A L V A F K I M S G E V P S T E D L V N L L P A I L S

GTGGCTGGCGCTCTGGTCGCCTTTAAGATTATGTCCGGCGAAGTGCCTAGCACAGAGGATCTGGTCAACCTCCTGCCATCTGTCC

HepCla #103

E L T P A E T T V R L R A Y M N T P G L P V C Q D H L E F W GAGCTCACCCCTGCCGAACCACAGTGAGACTGAGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCATCTGGAATCTGG

HepCla #186

P Q P E Y D L E L I T S C S S N V S V A H D G A G K R V Y Y CCCCAACCCGAATACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTAT

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HepCla #9

L G K V I D T L T C G F A D L M G Y I P L V G A P L G G A A CTGGGAAAGGTCATCGATACCCTCACCTGTGGCTTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCT

HepCla #93
AIPLEVIKGGRHLIFCHSKKKCDELAAKLV GCCATTCCCCTCGAGGTCATCAAAGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGCCAAACTGGTC

HepCla #112
G G V L A A L A A Y C L S T G C V V I V G R I V L S G K P A GGCGGAGTGCTCGCCGCTCTGGCTGCCTATTGCCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCT

C E S A G V Q E D A A S L R A F T E A M T R Y S A P P G D P TGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGGAGACCCT

G W F T A G Y S G G D I Y H S V S H A R P R W F W F C L L L GGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTC

S S S T S G I T G D N T T T S S E P A P S G C P P D S D A E AGCTCCAGCACAAGCGGAATCACAGGCGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGCGGATGCCCTCCCGATAGCGATAGCCGAA

T Q R R G R T G R G K P G I Y R F V A P G E R P S G M F D  ${\tt AGGACACAGGAGGGGAGGGAGGCAGGCAGGCAAACCCGGAATCTATAGGTTTGTGGCTCCCGGAGGGGACACCCTCCGGCATGTTCGAT}$ 

V R M Y V G G V E H R L E A A C N W T R G E R C D L E D R D GTGAGAATGTATGTGGGAGGCGTCGAGCATAGGCTCGAGGCTGCCTGTAACTGGACCAGAGGCGAAAGGTGTGACCTCGAGGATAGGGAT

E A O L H V W V P P L N V R G G R D A V I L L M C V V H P T GAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGCGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGTGCATCCCACA

L G V R A T R K T S E R S Q P R G R R Q P I P K A R P E G CTGGGAGTGAGAGCCACAAGGAAAACCTCCGAGAGAAAGCCAACCCAGAGGCAGAAGGCAACCCATTCCCAAAGCCAGAAGGCCTGAGGGA

N V S V A H D G A G K R V Y Y L T R D P T T P L A R A A W E AACGTCAGCGTCGCCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACACCCCTCGCCAGAGCCGCTTGGGAA

E P A P S G C P P D S D A E S Y S S M P P L E G E P G D P AGCGAACCCGCTCCCTCCGCCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGGAGACCCT

I G G H Y V Q M A I I K L G A L T G T Y V Y N H L T P L R D ATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGAT

PSTEDLV N LL PAILS PGALV V G V V C A A I L R  $\tt CCCTCCACCGAAGACCTCGTGAATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTGGGAGTGGTCTGCGCTGCCATTCTGAGA$ 

HepCla #24
I L D M I A G A H W G V L A G I A Y F S M V G N W A K V L V 

EGCGWAGWLLSPRGSRPSWGPTDPRRSSRN GAGGGATGCGGATGGCTGGCTGCTCAGCCCTAGGGGAAGCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAAT

HepCla #21 W T T Q G C N C S I Y P G H I T G H R M A W D M M M N W S P TGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCACAGGCCATAGGATGGCCCTGGGACATGATGATGAACTGGAGCCCT

V A M T P T V A T .R D G K L P A T Q L R R H I D L L V G S 

HepCla #42

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R L W H Y P C T I N Y T I F K V R M Y V G G V E H R L E A A AGGCTCTGGCATTACCTTGCACAATCAATTACACAATCTTTAAGGTCAGGATGTACGTCGGCGGAGTGGAACACAGACTGGAAGCCGCT

HepCla #172 V F C V Q P E K G G R K P A R L I V F P D L G V R V C E K M GTGTTTTGCGTCCAGCCTGAGAAAGGCGGAAGGAAACCCGCTAGGCTCATCGTCTTCCCTGACCTCGGCGTCAGGGTCTGCGAAAAGATG

HepCla #10

M G Y I P L V G A P L G G A A R A L A H G V R V L E D G V N

ATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGAGGCCCTGCCAGAGCCCCATGGCGTCAGGGTCCTGGAAGACGGAGTGAAT

HepCla #27
G G N A G R T T S G L V S L L T P G A K Q N I Q L I N T N G
GGCGGAAACGCTGGCAGAACCACAAGCGGACCTCGTCAGCCCCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGGA

HepCla #13

L A L L S C L T V P A S A Y Q V R N S T G L Y H V T N D C P

CTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCT

HepCla #71
G R D K N Q V E G E V Q I V S T A A Q T F L A T C I N G V C
GGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGT

HepCla #18

P A T Q L R R H I D L L V G S A T L C S A L Y V G D L C G S

CCCGCTACCCACTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTGTGGCTCC

HepCla #83

H A P T G S G K S T K V P A A Y A A Q G Y K V L V L N P S V
CACGCTCCCACAGGCTCCGGCAAAAGCACAAAGGTCCCCGCTGCCTATGCCGCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTC

 HepCla #6

 R T W A Q P G Y P W P L Y G N E G C G W A G W L L S P R G S

 AGGACATGGGCTCAGCCTGTCCCCCAGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCC

HepCla #162 T E D V V C C S M S Y S W T G A L V T P C A A E E Q K L P I ACCGAAGACGTCGTGTGTTGCTCCTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCCGAAGAGCAAAAGCTCCCCATT

HepCla #55
A L D T E V A A S C G G V V L V G L M A L T L S P Y Y K R Y
GCCCTCGACACAGAGGTCGCCGCTAGCTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTAT

HepCla #168
S V E E A C S L T P P H S A K S K F G Y G A K D V R C H A R
AGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTTCGAGTTTGGCTATGGCGCTAAGGATGTGAGATGCCATGCCAGA

HepCla #119
I S G I Q Y L A G L S T L P G N P A I A S L M A F T A A V T
ATCTCCGGCATTCAGTATCTGGCTGGCCTCAGCACACTGCCTGGCAATCCCGCTATCGCTAGCCTCATGGCTTCACAGCCGCTGTGACA

HepCla #3
Q I V G G V Y L L P R R G P R L G V R A T R K T S E R S Q P
CAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCCTAGGCTCAGGGCTACCAGAAAGACAAGCGAAAGGTCCCAGCCT

HEPCIA #194
L H S Y S P G E I N R V A A C L R K L G V P P L R A W R H R
CTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGAGACACAGA

HepCla #189

T A R H T P V N S W L G N I I M F A P T L W A R M I L M T H
ACCGCTAGGCATACCCCTGTGAATAGCTGGCTGGGAAACATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCAT

HepCla #81
ENLETTMRSPVFTDNSSPPAVPQSFQVAHL
GAGAATCTGGAAACCACAATGAGAAGCCCTGTGTTTTACCGATAACTCCAGCCCTCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTC

HepCla #91 ATPPGSVTVPHPNIEEVALSTTGEIPFYGK

PCT/AU01/00622 WO 01/090197

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 ${\tt GCCACACCCCTGGCTCCGTGACAGTGCCTCACCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAA}$ 

HepCla #60 L V F D I T K L L L A V F G P L W I L Q A S L L K V P Y F V CTGGTCTTCGATATCACAAAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGTC

T A A L V M A Q L L R I P Q A I L D M I A G A H W G V L A G ACCGCTGCCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAGTGCTCGCCGGA

HepCla #98
C N T C V T Q T V D F S L D P T F T I E T T T L P Q D A V S
TGCAATACCTGTGTGACACAGACAGTGGATTCTCCCTGGATCCCACATTCACAATCGAAACCACAACCCTCCCCCAAGACGCTGTGTCC

H G P T P L L Y R L G A V Q N E V T L T H P V T K Y I M T C  ${\tt CACGGACCCACACCCCTCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACTGACACACCCTGTGACAAAGTATATCATGACCTGT}$ 

ARVAIKSLTERLYVGGPLTNSRGENCGYRR GCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACCCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGA

C V I G G A G N N T L H C P T D C F R K H P E A T Y S R C G TGCGTCATCGGAGGCGCTGGCAATAACACACTGCATTGCCCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGA

HepCla #76
T C G S S D L Y L V T R H A D V I P V R R R G D S R G S L L 

HepCla #138
N M W S G T F P I N A Y T T G P C T P L P A P N Y T F A L W AACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCGCTCCCAATTACACATTCGCTCTGTGG

H S T D A T S I L G I G T V L D Q A E T A G A R L V V L A T CACTCCACCGATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTCGCCACA Y V P E S D A A A R V T A I L S S L T V T Q L L R R L H Q W TACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGACTGCATCAGTGG

HepCla#8
RPSWGPTDPRRRSRNLGKVIDTLTCGFADL AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACACTGACATGCGGATTCGCTGACCTC

HepCla #33 G P .D Q R P Y C W H Y P P K P C G I V P A K S V C G P V Y C 

E E C S Q H L P Y I E Q G M M L A E Q F K Q K A L G L L Q T GAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACA

Y Q A T V C A R A Q A P P P S W D Q M W K C L I R L K P T L TACCAAGCCACAGTGTGTGCCAAGCCCCTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTC

HepCla #161
D L S D G S W S T V S S E A G T E D V V C C S M S Y S W T G
GACCTCAGCGATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGTAGCATGAGCTATAGCTGGACCGGA

W D O M W K C L I R L K P T L H G P T P L L Y R L G A V Q N TGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAGCCGTCCAGAAT

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HepCla #116

L A E Q F K Q K A L G L L Q T A S R Q A E V I A P A V Q T N

CTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGGTCATCGCTCCCGCTGTGCAAACCAAT

HepCla #118

W Q K L E V F W A K H M W N F I S G I Q Y L A G L S T L P G
TGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTCATTAGCGGAATCCAATACCTCGCCGGACTGTCCACCCTCCCCGGA

HepCla #129
L I A F A S R G N H V S P T H Y V P E S D A A A R V T A I L
CTGATTGCCTTTGCCTCCAGGGGAACCATGTGTCCCCCACACACTATGTGCCTGAGTCCGACGCTGCGCTAGGGTCACCGCTATCCTC

HepC1a #19
A T L C S A L Y V G D L C G S V F L V G Q L F T F S P R R H
GCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGCGGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCAT

HepCla #102 S S V L C E C Y D A G C A W Y E L T P A E T T V R L R A Y M AGCTCCGTGCTCTGCGAATGCTATGACGCTGGCTGTGCCTGGTACGAACTGACACCCGCTGAGACAACCGTCAGGGCTCAGGGCTTACATG

HepCla #122
G W V A A Q L A A P G A A T A F V G A G L A G A A I G S V G
GGCTGGCTGCCCACTGCCCTGCCACAGCCTTTGTGGGAGCCGGACTGGCTGCCATTGGCTCCGTGGGA
GGCTGGCTGCCCACTGCCCACAGCCTTTGTGGGAGCCGGACTGGCTGCCATTGGCTCCGTGGGA

HepCla #29
SWHINSTALNCNESLNTGWLAGLFYQHKFN
AGCTGGCACATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAAT

HepCla #1
A A M S T N P K P Q R K T K R N T N R R P Q D V K F P G G G
GCCGCTATGTCCACATCCCAAACCCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGAGGCGGA

HepCla #36

A P T Y S W G A N D T D V F V L N N T R P P L G N W F G C T

GCCCCTACCTATAGCTGGGGCGCTAACGATACCGATGTGTTTGTGCTCAACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACA

HepCla #156
V P P P R K K R T V V L T E S T L S T A L A E L A T K S F G
GTGCCTCCCCCTAGGAAAAAAGAGAACCGTCGTCCTCACCGAAAGCACACTGTCCACCGCTCTGGCTGAGCTCGCCACAAAGTCCTTCGGA

HepCla #165
S T T S R S A C Q R Q K K V T F D R L Q V L D S H Y Q D V L
AGCACAACCTCCAGGTCCGCCTGTCAGAGACAGAAAAAGGTCACCTTTGACAGACTGCCAAGTGCTCGACTCCCACTATCAGGATGTGCTC

HepCla #90

D Q A E T A G A R L V V L A T A T P P G S V T V P H P N I E
GACCAAGCCGAAACCGCTGGCCTAGGCTCGGGTCCCGGTACCCCTCCCGGAAGCGTCACCCCATCCCCATATCGAA

HepCla #117
A S R Q A E V I A P A V Q T N W Q K L E V F W A K H M W N F
GCCTCCAGGCAAGCCGAAGTGATTGCCCCTGCCGTCCAGACAAACTGGCAGAAACTGGAAGTGTTTTGGGCTAAGCATATGTGGAACTTT

HepCla #181 C R A S G V L T T S C G N T L T C Y I K A R A A C R A A G L TGCAGAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTGGCCTC

PCT/AU01/00622 WO 01/090197

#### 137/216

F D R L O V L D S H Y Q D V L K E V K A A A S K V K A N L L TTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAGAGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTC

G P L T N S R G E N C G Y R R C R A S G V L T T S C G N T L GGCCTCTGACAAACTCCAGGGGAGAGAATTGCGGATACAGAAGGTGTAGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTC

HepCla #136
I M H T R C H C G A E I T G H V K N G T M R I V G P R T C R ATCATGCACACAAAGGTGTCACTGTGGCGCTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGA

HepCla #144
E V S F R V G L H E Y P V G S Q L P C E P E P D V A V L T S GAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCC

HepCla #167
K E V K A A A S K V K A N L L S V E E A C S L T P P H S A K AAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGCTTGCTCCCTGACACCCCCTCACTCCGCCAAA

HepCla #59
GRDAVILLMCVVHPTLVFDITKLLLAVFGP GGCAGAGACGCTGTGATTCTGCTCATGTGTGTGGTCCACCCTACCCTCGTGTTTGACATTACCAAACTGCTCCTGGCTGTTTTGGCCCT

HepCla #146
MLT DPSHITAEAAGRRLARGSPPSMASSSA 

PRPISYLKGSSGGPLLCPAGHAVGIFRAA AGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGCTGGCCATGCCGTCGGCATTTTCAGAGCCGCT

HepC1a #32
D F D Q G W G P I S Y A N G S G P D Q R P Y C W H Y P P K P GACTITGACCAAGGCTGGGGCCCTATCCCCTAACGGAAGCGGACCCGATCAGAGACCCTATTGCTGGCACTATCCCCCTAAGCCT

HepCla #128 R H V G P G E G A V Q W M N R L I A F A S R G N H V S P T H AGGCATGTGGGACCCGGAGAGGGAGCCGTCCAGTGGATGAATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCTACCCAT

HepCla #50

C L W M M L L I S Q A E A A L E N L V I L N A A S L A G T H TGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCAT

HepCla #114

I I P D R E V L Y R E F D E M E E C S Q H L P Y I E Q G M M ATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATG

HepCla #47

LIH L H Q N I V D V Q Y L Y G V G S S I A S W A I K W E Y CTGATTCACCTCCACAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTAT

HepCla #200

V S H A R P R W F W F C L L L A A G V G I Y L L P N R A A GTGTCCCACGCTAGGCCTAGGTGGTTCTGGTTCTGCTCCTGCTCGCCGCTGGCGTCGGCATTTACCTCCTGCCTAACAGAGCCGCT

A T L G F G A Y M S K A H G I D P N I R T G V R T I T T G GCCGCTACCCTCGGCTTTGGCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGA

RVQGLLRICALARKMIGGHYVQMAIIKLGA AGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCT

HepCla #153 R R F A Q A L P V W A R P D Y N P P L V E T W K K P D Y E P AGGAGATTCGCTCAGGCTCTGCCTGTGTGGGCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTGACTATGAGCCT

T A A Q T F L A T C I N G V C W T V Y H G A G T R T I A S P ACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGACCGTCTACCATGGCGCTGGCACAAGGACAATCGCTAGCCCT

HepCla #65

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W A H N G L R D L A V A V E P V V F S Q M E T K L I T W G A TGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTCGTGTTTAGCCAAATGGAACCAAACTGATTACCTGGGGCGCT

HepCla #64

L T G T Y V Y N H L T P L R D W A H N G L R D L A V A V E P

CTGACAGGCACATACGTCTACAATCACCTCACCCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGCCGTCGAGGCCT

HepCla #80

V C T R G V A K A V D F I P V E N L E T T M R S P V F T D N

GTGTGTACCAGAGGCGTCGCCAAAGCCGTCGACTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT

HepCla #95
A L G I N A V A Y Y R G L D V S V I P T S G D V V V A T D
GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGTGTCCCTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGAT

HepCla #111

M S A D L E V V T S T W V L V G G V L A A L A A Y C L S T G
ATGTCCGCCGATCTGGAGTGGTCACCTCCACCTGGGTGCTCGTGGGAGGGTGCTCCTGGCTGCCCCTGGCTGCCCTGGCTGCCCGCGGA

HepCla #97
A L M T G Y T G D F D S V I D C N T C V T Q T V D F S L D P
GCCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACCGTCGACTTTAGCCTCGACCCT

HepCla #2

N T N R R P Q D V K F P G G G Q I V G G V Y L L P R R G P R
AACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGGGGGGTGTATCTGCTCCCCAGAAGGGGACCCAGA

 HepCla #11

 R A L A H G V R V L E D G V N Y A T G N L P G C S F S I F L

 AGGGCTCTGGCTCACGGAGTGCTCGAGGATGGCGTCAACTATGCCACAGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTC

HepCla #169
S K F G Y G A K D V R C H A R K A V A H I N S V W K D L L E
AGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCACGCTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAA

HepC1a #28T P G A K Q N I Q L I N T N G S W H I N S T A L N C N E S L ACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCAATGGCTCCTGGCATATCAATAGCACAGCCCTCAACTGTAACGAAAGCCTC

HepCla #30

N T G W L A G L F Y Q H K F N S S G C P E R L A S C R R L T

AACACAGGCTGGCTGGCTGTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGAGAGACTGACACA

HepCla #49

V V L L F L L L A D A R V C S C L W M M L L I S Q A E A A L

GTGGTCCTGCTCTCCTCGCCGATGCCAGAGTGTTAGCTGTTGTGGATGATGCTGCTCATCTCCCAGGCTGAGGCTGCCCTC

HepCla #192

D C E I Y G A C Y S I E P L D L P P I I Q R L H G L S A F S GACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCCTATCATTCAGAGACTGCATGGCCTCAGCGCTTTCTCC

HepCla #73
W T V Y H G A G T R T I A S P K G P V I Q M Y T N V D Q D L
TGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGGATGTACACAAACGTCGACCAAGACCTC

HepCla #101 Y R F V A P G E R P S G M F D S S V L C E C Y D A G C A W Y TACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCTTGTGAGTGTTACGATGCCGGATGCGCTTGGTAT

HepCla #45 R S E L S P L L S T T Q W Q V L P C S F T T L P A L S T G AGGTCCGAGCTCAGCCCTCTGCTCCACCACCACCAGTGGCAGGTCCTGCTCCTTCACAACCCTCCCCGCTCTGTCCACCGGA

HepCla #195 LRKLG V P P L R A W R H R A R S V R A R L L A R G G R A

PCT/AU01/00622 WO 01/090197

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HepCla #121 SPLTTSQTLLFNILGGWVAAQLAAPGAATA AGCCCTCTGACAACCTCCCAGACACTGCTCTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCT

LWILQASLLKVPYFVRVQGLLRICALARKM CTGTGGATCCTCCAGGCTAGCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATG

V K N G T M R I V G P R T C R N M W S G T F P I N A Y T T G GTGAAAAACGGAACCATGAGGATTGTGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGGA

E V A L S T T G E I P F Y G K A I P L E V I K G G R H L I  ${\tt GAGGTCGCCCTCAGCACAACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTT}$ 

LTRDPTTPLARAAWETARHTPVNSWLGNII 

RVSAEEYVEIRRVGDFHYVTGMTTDNLKCP AGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTATGTGACAGGCATGACCACAGACAATCTGAAATGCCCT

HepCla #155
P V V H G C P L P P P R S P P V P P R K K R T V V L T E S 

HepCla #157
T L S T A L A E L A T K S F G S S S T S G I T G D N T T T S ACCCTCAGCACAGCCCTCGCCGAACTGGCTACCAAAAGCTTTGGCTCCAGCTCCAGCTCCGGCATTACCGGAGACAATACCACAACCTCC

HepCla #135 V V S C Q R G Y K G V W R G D G I M H T R C H C G A E I T G H GTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGGAGCCGAAATCACAGGCCAT

FLVGQLFTFSPRRHWTTQGCNCSIYPGH GTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTATCCCGGACACATT

F V G A G L A G A A I G S V G L G K V L V D I L A G Y G A G 

D I W D W I C E V L S D F K T W L K A K L M P Q L P G I P F GACATTTGGGATTGGGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCAAACTGATGCCCCAACTGCCTGGCATTCCCTTT

N S S I V Y E A A D A I L H T P G C V P C V R E G N A S R C AACTCCAGCATTGTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGT

HepCla #31 S S G C P E R L A S C R R L T D F D Q G W G P I S Y A N G S AGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCC

HepCla #178
R T E E A I Y Q C C D L D P Q A R V A I K S L T E R L Y V G AGGACAGAGGAAGCCATTTACCAATGCTGTGACCTCGACCCTCAGGCTAGGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGA

HepCla #69
V S K G W R L L A P I T A Y A Q Q T R G L L G C I I T S L T GTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACAGCCTATGCCCAACAGACAAGGGGGACTGCTCGGCTGTATCATTACCTCCCTGACA

HepCla #191
F F S V L I A R D Q L E Q A L D C E I Y G A C Y S I E P L D TTCTTTAGCGTCCTGATTGCCAGAGACCAACTGGAACAGGCTCTGGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGAT

C Q V P S P E F F T E L D G V R L H R F A P P C K P L L R E 

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- HepCla #86
  I D P N I R T G V R T I T T G S P I T Y S T Y G K F L A D G
  ATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTCTGGCTGACGGA
- HepCla #44

  C N W T R G E R C D L E D R D R S E L S P L L L S T T Q W Q

  TGCAATTGGACAAGGGGAGAGAGATGCGATCTGGAAGACAGAAGCGAACTGTCCCCCCTCCTGCTCAGCACAACCCAATGGCAA
- HepCla #22

  T G H R M A W D M M M N W S P T A A L V M A Q L L R I P Q A

  ACCGGACACAGAATGGCTTGGGATATGATGATGATGATTGGTCCCCCACAGCCGCTCTGGTCATGGCTCAGCTCCTGAGAATCCCTCAGGCT
- HepCla #127

  P G A L V V G V V C A A I L R R H V G P G E G A V Q W M N R

  CCCGGAGCCCTCGTGGTCGGCGTGTGTGCCCCTATCCTCAGGAGACACGTCGGCCCTGGCGAAGGCGCTGTGCAATGGATGAACAGA
- HepCla #149 H D S P D A E L I E A N L L W R Q E M G G N I T R V E S E N CACGATAGCCCTGACGCTCATCCGAAGCCAATCTGCTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAAT
- HepCla #5

  R G R R Q P I P K A R R P E G R T W A Q P G Y P W P L Y G N
  AGGGGAAGGAGACCCTATCCCTAAGGCTAGGAGACCCGAAGCCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAAT
- HepCla #173 L I V F P D L G V R V C E K M A L Y D V V S K L P L A V M G CTGATTGTGTTTCCCGATCTGGGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCCTCGCCGTCATGGGA
- HepCla #124
  L G K V L V D I L A G Y G A G V A G A L V A F K I M S G E V
  CTGGGAAAGGTCCTGGTCGACATTCTGGCTGGCTATGGCGCTCGCCGGAGCCCTCGTGGCTTTCAAAATCATGAGCGGAGAGGTC
- HepCla #160
  S Y S S M P P L E G E P G D P D L S D G S W S T V S S E A G
  AGCTATAGCTCCATGCCTCCCCTCGAGGGAGAGCCTGGCGATCCCGATCTGTCCGACGGAAGCTGGAGCACAGTGTCCAGCGAAGCCGGA
- HepCla #150
  R Q E M G G N I T R V E S E N K V V I L D S F D P L V A E E AGGCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAGCGAAAACAAAGTGGTCATCCTCGACTCCTTCGATCCCCTCGTGGCTGAGGAA
- HepCla #75
  V G W P A P Q G S R S L T P C T C G S S D L Y L V T R H A D
  GTGGGATGGCCTCACCCCTCAGGGAAGCCAGAAGCCTCACCCCTTGCACATGCGAAGCTCCGACCTCTACCTCGTGACAAGGCATGCCGAT
- HepCla #88

  G C S G G A Y D I I I C D E C H S T D A T S I L G I G T V L
  GGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTC
- HepCla #99 T F T I E T T T L P Q D A V S R T Q R R G R T G R G K P G I ACCTITACCATTGAGACCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGAGCCAGAACCGGAAGGGGAAAGCCTGGCATT
- HepCla #40

  D C F R K H P E A T Y S R C G S G P W I T P R C L V D Y P Y GACTGTTTCAGAAAGCATCCCGAAGCCATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTCGTCGACTATCCCTAT
- HepCla #201 L A A G V G I Y L L P N R A A CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCC

### 141/216

HepCla #163
A L V T P C A A E E Q K L P I N A L S N S L L R H H N L V Y
GCCCTCGTGACACCCTGTGCCGCTGAGGAACAGAAACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCATAACCTCGTGTAT

HepCla #132
I S S E C T T P C S G S W L R D I W D W I C E V L S D F K T
ATCTCCAGCGAATGCACACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGATCTGTGAGGTCCTGTCCGACTTTAAGACA

HEPCIA #134

W L K A K L M P Q L P G I P F V S C Q R G Y K G V W R G D G
TGGCTCAAGGCTAAGCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGGAGGGCTATAAGGGAGTGTGGAGGGGAGACGGA

S G P W I T P R C L V D Y P Y R L W H Y P C T I N Y T I F K
AGCGGACCCTGGATCACCCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACCATTTTCAAA

#### Artificial Protein:

VIPVRRRGDSRGSLLSPRPISYLKGSSGGPARRGREILLGPADGMVSKGWRLLAPITAYARLHRFAPPCKPLLREEVSFRVGLHEYPVGSVVFSQMET KLITWGADTAACGDIINGLPVSLLCPAGHAVGIFRAAVCTRGVAKAVDFIPVCVVIVGRIVLSGKPAIIPDREVLYREFDEMPCTPLPAPNYTFALWR VSAEEYVEIRRVGDALYDVVSKLPLAVMGSSYGFQYSPGQRVEFISWCLWWLQYFLTRVEAQLHVWVPPLNVRGENLVILNAASLAGTHGLVSFLVFF CFAWYLLPP1IQRLHGLSAFSLHSYSPGEINRVAACNPPLVETWKKPDYEPPVVHGCPLPPPRSPPGVGSSIASWAIKWEYVVLLFLLLADARVCSLN ntrpplgnwfgctwmnstgftkvcgappfteamtrysappgdppqpeydlelitscsswpllllllalpqrayaldtevaascggvvlqqtrgllgci ITSLTGRDKNQVEGEVQIVSSSPPAVPQSFQVAHLHAPTGSGKSTKVPAANTPGLPVCQDHLEFWEGVFTGLTHIDAHFLVLLLFAGVDAETHVTGGN agrttsglvsllevtlthpvtkyimtcmsadlevvtstwvlvvglmaltlspyykryiswclwwlqyfltrvaicgkylfnwavrtklkltpiaaagr LDLS1AYFSMVGNWAKVLVVLLLFAGVDAETHVTRLARGSPPSMASSSASQLSAPSLKATCTANGLVSFLVFFCFAWYLKGRWVPGAVYALYGMQLPC epepdvavltsmltdpshitaeaagrdsvtpidttimaknevfcvqpekggrkparyaaqgykvlvlnpsvaatlgfgaymskahgvrnstglyhvtn DCPNSSIVYEAADAILHTSSYGFQYSPGQRVEFLVQAWKSKKTPMGFSDTAACGDIINGLPVSARRGREILLGPADGMSQLSAPSLKATCTANHDSPD aelieanllwnpaiaslmaftaavtsplitsqtllfnilglvqawkskktpmgfsydtrcfdstvtesdidereisvpaeilrksrrpaqalpvwarp DYMFAPTLWARMILMTHFFSVLIARDQLEQALSVIPTSGDVVVVATDALMTGYTGDFDSVIDCHSKKKCDELAAKLVALGINAVAYYRGLDVVLPCSF TTLPALSTGLIHLHONIVDVOYLYKGRWVPGAVYALYGMWPLLLLLLALPQRAYSPITYSTYGKFLADGGCSGGAYDIIICDECARSVRARLLARGGR AAICGKYLFNWAVRTKKAVAHINSVWKDLLEDSVTPIDTTIMAKNEFTPSPVVVGTTDRSGAPTYSWGANDTDVFVPGCVPCVREGNASRCWVAMTPT VATROGKLODCTMLVCGDDLVVICESAGVQEDAASLRAVAGALVAFKIMSGEVPSTEDLVNLLPAILSYDTRCFDSTVTESDIRTEEAIYQCCDLDPQ ELTPAETTVRLRAYMVTPGLPVCQDHLEFWPQPEYDLELITSCSSNVSVAHDGAGKRVYYLGKVIDTLTCGFADLMGYIPLVGAPLGGAAAIPLEVIK GGRHLIFCHSKKKCDELAAKLVGGVLAALAAYCLSTGCVVIVGRIVLSGKPACESAGVQEDAASLRAFTEAMTRYSAPPGDPGWFTAGYSGGDIYHSV sharprwfwfclllssstsgitgdntttssepapsgcppdsdaertqrrgrtgrgkpgiyrfvapgerpsgmfdvrmyvggvehrleaacnwtrgerc  ${\tt DLEDRDEAQLHVWVPPLNVRGGRDAVILLMCVVHPTLGVRATRKTSERSQPRGRRQPIPKARRPEGNVSVAHDGAGKRVYYLTRDPTTPLARAAWESE}$ PAPSGCPPDSDAESYSSMPPLEGEPGDPIGGHYVQMAIIKLGALTGTYVYNHLTPLRDPSTEDLVNLLPAILSPGALVVGVVCAAILRILDMIAGAHW  ${\tt GVLAGIAYFSMVGNWAKVLVEGCGWAGWLLSPRGSRPSWGPTDPRRRSRNWTTQGCNCSIYPGHITGHRMAWDMMMNWSPWVAMTPTVATRDGKLPAT}$ QLRRHIDLLVGSRLWHYPCTINYTIFKVRMYVGGVEHRLEAAVFCVQPEKGGRKPARLIVFPDLGVRVCEKMMGYIPLVGAPLGGAARALAHGVRVLE DGVNGGNAGRTTSGLVSLLTPGAKQNIQLINTNGLALLSCLTVPASAYQVRNSTGLYHVTNDCPGRDKNQVEGEVQIVSTAAQTFLATCINGVCPATQ LRRHIDLLVGSATLCSALYVGDLCGSHAPTGSGKSTKVPAAYAAQGYKVLVLNPSVRTWAQPGYPWPLYGNEGCGWAGWLLSPRGSTEDVVCCSMSYS WTGALVTPCAAEEQKLP1ALDTEVAASCGGVVLVGLMALTLSPYYKRYWMNSTGFTKVCGAPPCV1GGAGNNTLHCPTSVEEACSLTPPHSAKSKFGY GAKDVRCHAR I SGIQYLAGLSTLPGNPAIASLMAFTAAVTQI VGGVYLLPRRGPRLGVRATRKTSERSQPLHSYSPGEINRVAACLRKLGVPPLRAWR HRTARHTPVNSWLGNIIMFAPTLWARMILMTHENLETTMRSPVFTDNSSPPAVPQSFQVAHLATPPGSVTVPHPNIEEVALSTTGEIPFYGKLVFDIT KLLLAVFGPLWILQASLLKVPYFVTAALVMAQLLRIPQAILDMIAGAHWGVLAGCNTCVTQTVDFSLDPTFTIETTTLPQDAVSHGPTPLLYRLGAVQ NEVTLTHPVTKYIMTCARVAIKSLTERLYVGGPLTNSRGENCGYRRCVIGGAGNNTLHCPTDCFRKHPEATYSRCGTCGSSDLYLVTRHADVIPVRRR GDSRGSLLNMWSGTFPINAYTTGPCTPLPAPNYTFALWHSTDATSILGIGTVLDQAETAGARLVVLATYVPESDAAARVTAILSSLTVTQLLRRLHQW RPSWGPTDPRRRSRNLGKVIDTLTCGFADLGPDQRPYCWHYPPKPCGIVPAKSVCGPVYCEECSQHLPYIEQGMMLAEQFKQKALGLLQTYQATVCAR AOAPPPSWDOMWKCLIRLKPTLCGIVPAKSVCGPVYCFTPSPVVVGTTDRSGSSLTVTQLLRRLHQWISSECTTPCSGSWLRDLSDGSWSTVSSEAGT EDVVCCSMSYSWTGWDQMWKCLIRLKPTLHGPTPLLYRLGAVQNLAEQFKQKALGLLQTASRQAEVIAPAVQTNWQKLEVFWAKHMWNFISGIQYLAG LSTLPGLI AFASRGNHVSPTHYVPESDAAARVTA I LATLCSALYVGDLCGSVFLVGQLFTFSPRRHSSVLCECYDAGCAWYELTPAETTVRLRAYMGW VAAQLAA PGAATAFVGAGLAGAA IGSVGSWHINSTALNCNESLNTGWLAGLFYQHKFNNALSNSLLRHHNLVYSTTSRSACQRQKKVTAAMSTNPKPQ RKTKRNTNRRPQDVKFPGGGSQTKQSGENFPYLVAYQATVCARAQAPPPSAPTYSWGANDTDVFVLNNTRPPLGNWFGCTVPPPRKKRTVVLTESTLSTALAELATKSFGSTTSRSACQRQKKVTFDRLQVLDSHYQDVLDQAETAGARLVVLATATPPGSVTVPHPN1EFHYVTGMTTDNLKCPCQVPSPEFFTE LDGVLKLTP1AAAGRLDLSGWFTAGYSGGD1YHSASRQAEV1APAVQTNWQKLEVFWAKHMWNFCRASGVLTTSCGNTLTCY1KARAACRAAGLFDRL QVLDSHYQDVLKEVKAAASKVKANLLGPLTNSRGENCGYRRCRASGVLTTSCGNTLIMHTRCHCGAEITGHVKNGTMRIVGPRTCREVSFRVGLHEYP vgsqlpcepepdvavltskevkaaaskvkanllsveeacsltpphsakgrdavillmcvvhptlvfditklllavfgpmltdpshitaeaagrrlarg SPPSMASSSASPRPISYLKGSSGGPLLCPAGHAVGIFRAADFDQGWGPISYANGSGPDQRPYCWHYPPKPRHVGPGEGAVQWMNRLIAFASRGNHVSP THCLWMMLLISQAEAALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHONIVDVQYLYGVGSSIASWAIKWEYVSHARP rwfwfcllllaagvgiyllpnraaaatigfgaymskahgidpnirtgvrtittgrvqgllricalarkmigghyvqmaiiklgarrfaqalpvwarpd YNPPLVETWKKPDYEPTAAQTFLATCINGVCWTVYHGAGTRTIAS PWAHNGLRDLAVAVEPVVFSQMETKLITWGAKGPVIQMYTNVDQDLVGWPAPQ GSRSLTPCKVVILDSFDPLVAEEDEREISVPAEILRKSLTGTYVYNHLTPLRDWAHNGLRDLAVAVEPVCTRGVAKAVDFIPVENLETTMRSPVFTDN vkfpgggqivggvyllprrgprrlahgvrvledgvnyatgnlpgcsfsiflskfgygakdvrcharkavahinsvwkdlletpgakqniqlintngs whinstalncneslntgwlaglfyqhkfnssgcperlascrrutvvllfllladarvcsclwmmllisqaeaaldceiygacysiepldlppiiqrlh  ${\tt GLSAFSWTVYHGAGTRTIASPKGPVIQMYTNVDQDLYRFVAPGERPSGMFDSSVLCECYDAGCAWYRSELSPLLLSTTQWQVLPCSFTTLPALSTGLR}$ klgvpplrawrhrarsvrarllarggrasplttsqtllfnilggwvaaqlaapgaatalwilqasllkvpyfvrvqgllriCalarkmvkngtmrivg PRTCRNMWSGTFPINAYTTGEVALSTTGEIPFYGKAIPLEVIKGGRHLIFLTRDPTTPLARAAWETARHTPVNSWLGNIIRVSAEEYVEIRRVGDFHY VTGMTTDNLKCPPVVHGCPLPPPRSPPVPPPRKKRTVVLTESTLSTALAELATKSFGSSSTSG1TGDNTTTSVSCQRGYKGVWRGDG1MHTRCHCGAE  ${\tt ITGHVFLVGQLFTFSPRRHWTTQGCNCSIYPGHIFVGAGLAGAAIGSVGLGKVLVDILAGYGAGDIWDWICEVLSDFKTWLKAKLMPQLPGIPFNSSI$ VYEAADAILHTPGCVPCVREGNASRCSSGCPERLASCRRLTDFDQGWGPISYANGSRTEEAIYQCCDLDPQARVAIKSLTERLYVGVSKGWRLLAPIT AYAQQTRGLLGCIITSLTFFSVLIARDQLEQALDCEIYGACYSIEPLDCQVPSPEFFTELDGVRLHRFAPPCKPLLRETCYIKARAACRAAGLQDCTM

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LVCGDDLVVIIDPNIRTGVRTITTGSPITYSTYGKFLADGCNWTRGERCDLEDRDRSELSPLLLSTTQWQTGHRMAWDMMMNWSPTAALVMAQLLRIP QAPGALVVGVVCAAILRRHVGPGEGAVQWMNRHDSPDAELIEANLLWRQEMGGNITRVESENEGVFTGLTHIDAHFLSQTKQSGENFPYLVARGRRQP IPKARRPEGRTWAQPGYPWPLYGNLIVFPDLGVRVCEKMALYDVVSKLPLAVWGYATGNLPGCSFSIFLLALLSCLTVPASAYQLGKVLVDILAGYGA GVAGALVAFKIMSGEVSYSSMPPLEGEPGDPDLSDGSWSTVSSEAGRQEMGGNITRVESENKVVILDSFDPLVAEEVGWPAPQGSRSLTPCTCGSSDLYLVTRHADGCSGGAYDIIICDECHSTDATSILGIGTVLTFTIETTTLPQDAVSRTQRRGRTGRGKPGIDCFRKHPEATYSRCGSGPWITPRCLVDYPY LAAGVGIYLLPNRAAALVTPCAAEEQKLPINALSNSLLRHHNLVYISSECTTPCSGSWLRDIWDWICEVLSDFKTWLKAKLMPQLPGIPFVSCQRGYK GVWRGDGSGPWITPRCLVDYPYRLWHYPCTINYTIFK

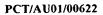
#### Artificial DNA:

GTGATTCCCGTCAGGAGAAGGGGAGACTCCAGGGGAAGCCTCCTGTCCCCCAGACCCATTAGCTATCTGAAAGGCTCCAGCGGAGGCCCTGCCAGAAG GGGAAGGGAAATCCTCCTGGGACCCGCTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCTGGCTCCCATTACCGCTTACGCTAGGCTCCACAGATTCG CTCCCCCTTGCAAACCCCTCCTGAGAGAGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCGGCTCCGTGGTCTTCTCCCCAGATGGAGACA CTTTAGGCTGCCGTCTGCACAAGGGGAGTGGCTAAGGCTGTGGATTTCATTCCCGTCTGCGTCGTGATTGTGGGAAGGATTGTGCTCAGCGGAAAGC GTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGATGCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGGCTCCAGCTATGG CTTTCAGTATAGCCCTGGCCAAAGGGTCGAGTTTATCTCCTGGTGTCTGTGGTGGCTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGT TGCTTTGCCTGGTACCTCCTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCCGGAGAGATTAACAGAGT GGCTGCCTGTAACCCTCCCCTCGTGGAAACCTGGAAGAAACCCGATTACGAACCCCCTGTGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCC  $\tt CTGGCGTCGGCTCCAGCATTGCCTCCTGGGCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGACGCTGACGCTTGGCTCCCTGAAT$ AACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCTTTCACAAGAGGCTAT TCGCCCTCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGGCTGCCTCCTGCGGAGGCGTCGTGCTCCAGCAAACCAGAGGGCCTCCTGGGATGCATT ATCACAAGCCTCACCGGAAGGGATAAGAATCAGGTCGAGGGAGAGGTCCAGATTGTGTCCAGCTCCCCCCTGCCGTCCCCCAAAGCTTTCAGGTCGC AAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTCGTGCTCCTCCTCCTCGTCGCCGCTCGACGCTGAGACACACGCTCACCGGAGGCAAT GGTCGTGACAAGCACATGGGTCCTGGTCGTGGGACTGATGGCCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGCCTCTGGTGGCTGC ANTACTTTCTGACAAGGGTCGCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGA CTGGATCTGTCCATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTCCTGTTTGCCGGAGTGGATGCCGAAACCCATGT TCGTGTCCTTCCTCGTGTTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATGCAGCTCCCCTGT GAGCCTGAGCCTGACGTCGCCGTCCTGACAAGCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGAGACTCCGTGACACCCCATTGA CACAACCATTATGGCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGATACGCTGCCCAAGGCTATAAGGTCCTGG TCCTGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGAGTGAGAAACTCCACCGGACTGTATCACGTCACCAAT GACTGTCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACAAGCTCCTACGGATTCCAATACTCCCCCGGACAGAGAGTGGAATT CCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCCGACACGCCGCTTGCGGAGACATTATCAATGGCCTCCCCGTCAGCGCTAGGA GAGGCAGAGAGATTCTGCTCGGCCCTGCCGATGGCATGAGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGAT GCCGAACTGATTGAGGCTAACCTCCTGTGGAACCCTGCCATTGCCTCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCCTCACCACAACCCAAAC CCTCCTGTTTAACATTCTGGGACTGGTCCAGGCTTGGAAAAGCAAAAAGACACCCATGGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGA GACTATATGTTTGCCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGGATCAGCTCGAGCAAGCCCTCAG CGTCATCCCTACCTCCGGCGATGTGGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGATTGCCATAGCA AAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTCGTCGCCCTGTAGCTTT ACCACACTGCCTGCCCTCAGCACAGGCCTCATCCATCTGCATCAGAATATCGTCGACGTCCAGTATCTGTATAAGGGAAGGTGGCTGCCTGGCGCTGT GTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTGCTCCTGCTCTGCCTCAGAGAGCCTATAGCCCTATCACATACTCCACCTATGGCAAATTCC TCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGTCCAGAAGCGTCAGGGCTAGGCTCCTGGCTAGGGGAGGCAGA GCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAAAAGGCTGTGGCTCACATTAACTCGGTGTGGAAGGATCTGCTCGAGGATAG CGTCACCCCTATCGATACCACAATCATGGCCAAAAACGAATTCACACCCTCCCCGTCGTGGTCGGCACAACCGATAGGTCCGGCGCTCCCACATACT CCTGGGGAGCCAATGACACAGACGTCTTCGTCCCCGGATGCGTCCCCTGTGTGAGAGAGGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACA GTGGCTACCAGAGACGGAAAGCTCCAGGATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGC GAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCATCTGGAATTCTGGCCCCAACC CGANTACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTATCTGGGAAAGGTCATCG ATACCCTCACCTGTGGCTTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCTGCCATTCCCCTCGAGGTCATCAAA GGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGCCAAACTGGTCGGCGGAGTGCTCGCCCTCTGGCTGCCTATTG CCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCTTGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGA AGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTCAGCTCCAGCACAAGCGGAATCACAGGCGATAACACAAACCACAAGCTCCGAGCCTGC GACCTCGAGGATAGGGATGAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGCGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGT GCATCCCACACTGGGAGTGAGAGCCACAAGGAAAACCTCCGAGAGAAGCCAACCCAGAGGCAGAAGGCAACCCATTCCCAAAGCCAGAAGGCCTGAGG GAAACGTCAGCGTCGCCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACACCCCTCGCCAGAGCCGCTTGGGAAAGCGAA CCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGGAGACCCTATCGGAGGCCATTA CGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGATCCCTCCACCGAAGACCTCGTGA ATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTGGGAGTGGTCTGCGCTGCCATTCTGAGAATCCTCGACATGATCGCTGGCGCTCACTGG GGGAAGCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAATTGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCA 

#### WO 01/090197

### 143/216

TCAGGGTCTGCGAAAAGATGATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGAGGCGCTGCCAGAGCCCTCGCCCATGGCGTCAGGGTCCTGGAA GACGGAGTGAATGGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCCAAACAGAATATCCAACTGATTAACACAAA CGGACTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCTGGCA GAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGTCCCGCTACCCAA CTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTGTGGCTCCCACGCGCTCCCACAGGCTCCGG CAAAAGCACAAAGGTCCCCGCTGCCTATGCCGCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTCAGGACATGGGCTCAGCCTGGCTATCCCT GGCCCCTCTACGGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCCACCGAAGACGTCGTGTTGTTGCTCCATGTCCTACTCC TGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCAAAAGCTCCCCATTGCCCTCGACACAGAGGTCGCCGCTAGCTGTGGCGGAGTGGTCCT TTGGCGGAGCCGGAAACAATACCCTCCACTGTCCCACAAGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCGCATAGCGCTAAGTCCAAGTTTGGCTAT GGCTTTCACAGCCGCTGTGACACAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCGGCGTCAGGGCTACCAGAAAGACAAGCG AAAGGTCCCAGCCTCTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGA GAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTCGCCACACCCC CTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAACTGGTCTTCGATATCACA AAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGTCACCGCTGCCCTCGTGATGGCCCAACT CCCTGGATCCCACATTCACAATCGAAACCACAACCCTCCCCCAAGACGCTGTGTCCCACGGACCCCACACCCCTCTGTATAGGCTCGGCGCTGTGCAA AACGAAGTGACACTGACACCCTGTGACAAAGTATATCATGACCTGTGCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACC CCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGATGCGTCATCGGAGGCGCTGGCAATAACACACTGCATTGCCCTACCGATTGCTTTAGGA AACACCCTGAGGCTACCTATAGCAGATGCGGAACCTGTGGCTCCAGCGATCTGTATCTGGTCACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGA GGCGATAGCAGAGGCTCCCTGCTCAACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCCTCCCCGCTCCCAATTA CACATTCGCTCTGTGGCACTCCACCGATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTGC TCGCCACATACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGACTGCATCAGTGG AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACACTGACATGCGGATTCGCTGACCTCGGCCCTGA ATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACATACCAAGCCACAGTGTGTGCCAGA GAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGATGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTAC CCCTCTGCTCTACAGACTGGGAGCCGTCCAGAATCTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGG TCATCGCTCCCGCTGTGCAAACCAATTGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCAATACCTCGCCGGA CTGTCCACCCTCCCGGACTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATGTGCCTGAGTCCGACGCTGCCGCTAGGGTCAC CGCTATCCTCGCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGCGGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGC ATAGCTCCGTGCTCTGCGAATGCTATGACGCTGGCTGTGCCTGGTACGACTGACACCCGCTGAGACACCGTCAGGCTCAGGGCTTACATGGGCTGG  $\tt CTCCACCGCTCTGAATTGCAATGGGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAATAACGCTCTGTCCAACTCCCTGCCAACTCCCTGCCAACTCCCTGCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAACTCAAC$ AGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGAGGCGGAAGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCTTCAACAATACCAGACCCCTCTGGGAAACTGGTTCGGATGCACAGTGCCTCCCCCTAGGAAAAAGAGAACCGTCGTGCTCACCGAAAGCACACTGTCC ACCGCTCTGGCTGAGCTCGCCACAAAGTCCTTCGGAAGCACAACCTCCAGGTCCGCCTGTCAGAGAAAAAGGTCACCTTTGACAGACTGCAAGT GCTCGACTCCCACTATCAGGATGTGCTCGACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCCTGGCTACCCCTACCCCTCCCGGAAGCGTCACCG TCCCCCATCCCAATATCGAATTCCATTACGTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCCGGAATTCTTTACCGAA GAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAAAGCCGGGGCGCTTGCAGAGCCGCTGGCCTCTTCGATAGGCTC CAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAGAGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTCGGCCCTCTGACAAACTCCAG GGGAGAGAATTGCGGATACAGAAGGTGTAGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTCATCATGCACACAAGGTGTCACTGTGGCG  $\tt CTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGAGAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCT$ GTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCCAAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCT AGCCCTCCTCCATGGCTAGCTCCAGCGCTAGCCCTAGCCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGCTGGCCATGC CGTCGGCATTTTCAGAGCCGCTGACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCGGACCCGATCAGAGACCCTATTGCTGGCACT ATCCCCCTAAGCCTAGGCATGTGGGACCCGGAGAGGGAGCCGTCCAGTGGATGAATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCT ACCCATTGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCCATAT CATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATGCTGATTCACC TCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTATGTGTCCCACGCTAGGCCT AGGTGGTTCTGGTTCTGCTCCTGCTCGCCGCTGGCGTCGGCATTTACCTCCTGCCTAACAGAGCCGCTGCCGCTACCCTCGGCTTTGGCGCTTA CATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGAAGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGG CTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCTAGGAGATTCGCTCAGGCTCTGCCTGTGTGGGCCAGACCCGAT TACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTGACTATGAGCCTACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGAC CGTCTACCATGGCGCTGGCACAAGGACAATCGCTAGCCCTTGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTCGTGTTTAGCC GATTCTGAGAAAGTCCCTGACAGGCACATACGTCTACAATCACCTCACCCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGCCG TCGAGCCTGTGTGTGCCAGAGGCGTCGCCAAAGCCGTCGACTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGATGTGTCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGATATGTCCGC



### 144/216

ATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACCGTCGACTTTAGCCTCGACCCTAACACAAACAGAAGGCCTCAGGAT GTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGAAGGGCTCTGGCTCACGGAGTGAGAGTGCTCGA GGATGGCGTCAACTATGCCACAGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTCAGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCACG CTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAAACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCAATGGCTCC TCATCTCCCAGGCTGAGGCTGCCCTCGACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCTATCATCAGAGACTGCAT GGCCTCAGCGCTTTCTCCTGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGA <u>CCAAGACCTCTACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTGTGAGTGTTACGATGCCGGATGCGCTTGGT</u> ATAGGTCCGAGCTCAGCCCTCTGCTCCTGTCCACACACAGTGGCAGGTCCTGCCTTGCTCCTTCACAACCCTCCCGGCTCTGTCCACCGGACTGAGA AAGCTCGGCGTCCCCCTCTGAGAGCCTGGAGGCATAGGGCTAGGTCCGTGAGAGCCCAGACTCCTCGCCAGAGGCGGAAGGGCTAGCCCTCTGACAAC CTCCCAGACACTGCTCTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCTCTGTGGATCCTCCAGGCTAGCC TCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATGGTGAAAAAACGGAACCATGAGGATTGTGGGA CCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGGAGAGGTCGCCCTCAGCACAACCGGAGAGATTCCCTTTTA CGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTTCTGACAAGGGATCCCACAACCCCTCTGGCTAGGGCTGCCTGGGAGA CAGCCAGACACACCCGTCAACTCCTGGCTCGGCAATATCATTAGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTAT GAAAAGGACAGTGGTCCTGACAGAGTCCACCCTCAGCACAGCCCTCGCCGAACTGGCTACCAAAAGCTTTGGCTCCAGCTCCACCTCCGGCATTACCG GAGACAATACCACAACCTCCGTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGGAGCCGAA ATCACAGGCCATGTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTATCCCGGACA CATTTTCGTCGGCGCTGGCCTCGCCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCGGAGACA <u>TTTGGGATTGGATTTGCGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCAAACTGATGCCCCAACTGCCTGGCATTCCCTTTAACTCCAGCATT</u> GTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGTAGCTCCGGCTGTCCCGAAAG GCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCCAGGACAGAGGAAGCCATTTACCAATGCT GTGACCTCGACCCTCAGGCTAGGGTCGCCATTAAGTCCCTGACAGAGAGCTGTATGTGGGAGTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACA GCCTATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACATTCTTTAGCGTCCTGATTGCCAGAGACCAACTGGAACAGGCTCT GGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGATTGCCAAGTGCCTAGCCCTGAGTTTTTCACAGAGCTCGACGGAGTGAGACTGC ATAGGTTTGCCCCTCCCTGTAAGCCTCTGCTCAGGGAAACCTGTTACATTAAGGCTTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATG CTGGTCTGCGGAGACGATCTGGTCGTGATTATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATA CAACCCAATGGCAAACCGGACACAGAATGGCTTGGGATATGATGATGATTGGTCCCCCACAGCCGCTCTGGTCATGGCTCAGCTCCTGAGAATCCCT CAGGCTCCCGGAGCCCTCGTGGTCGGCGTCGTGTGTGCCGCTATCCTCAGGAGACACGTCGGCCCTGGCGAAGGCGCTGTGCAATGGATGAACAGACA CGATAGCCCTGACGCTGAGCTCATCGAAGCCAATCTGCTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAATGAGGGAGTGT <u>TTACCGGACTGACACATTGACGCTCACTTTCTGTCCCAGACAAAGCAAAGCGGAGAGATTTCCCTTACCTCGTGGCTAGGGGAAGGAGACAGCCT</u> ATCCCTAAGGCTAGGAGACCCGAAGGCAGAACCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAATCTGATTGTGTTTCCCGATCTGGGAGT GAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCCTCGCCGTCATGGGATACGCTACCGGAAACCTCCCCGGATGCTCCTTCT GGCGTCGCCGGAGCCCTCGTGGCTTTCAAAATCATGAGCGGAGAGGTCAGCTATAGCTCCATGCCTCCGCGAGGGAGAGCCTGGCGATCCCGATCT GTCCGACGGAAGCTGGAGCACAGTGTCCAGCGAAGCCGGAAGGCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAGCGAAAACAAAGTGGTCATCC TCGACTCCTTCGATCCCCTCGTGGCTGAGGAAGTGGGATGGCCTGCCCCTCAGGGAAGCAGAAGCCTCACCCCTTGCACATGCGGAAGCTCCGACCTC TACCTCGTGACAAGGCATGCCGATGGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGG CATTGGCACAGTGCTCACCTTTACCATTGAGACAACCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGAGGCAGAACCGGAAGGGGAAAGG CTGGCATTGACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCCGCCCTCGTGACACCCTGTGCCGCTGAGGAACAGAAACTGCCTATCAATGCCCT CAGCAATAGCCTCCTGAGACACCATAACCTCGTGTATATCTCCAGCGAATGCACAACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGA TCTGTGAGGTCCTGTCCGACTTTAAGACATGGCTCAAGGCTAAGCTCATGCCTCAGCTCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGCTATAAG GGAGTGTGGAGGGGGAGACGGAAGCGGACCCTGGATCACACCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTA TACCATTTTCAAA

HepC Savine Cassette Sequences (A+B+C) with specific restriction sites removed which can be joined to generate a single expressible open reading frame that encodes the hepc Savine protein above

### Cassette A

### 145/216

CTGGGCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCCCTGAATAACACAA GGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCTTTC ACAGAGGCTATGACAAGGTATAGCGCTCCCCTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTG TAGCTCCTGGCTCCTGCTCCTGCTCCCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGGCTGCCTCCT GCGGAGGCGTCGTGCTCCAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAG GTCGAGGGAGAGGTCCAGATTGTGTCCAGCTCCCCCCTGCCGTCCCCCAAAGCTTTCAGGTCGCCCATCTGCATGCCCC TACCGGAAGCGGAAAGTCCACCAAAGTGCCTGCCGCTAACACCCCGGACTGCCTGTGTGTCAGGATCACCTCGAGTTTT GGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTCGTGCTCCTTGCTCTTCGCTGGCGTqGAŁGCTGAG ACACACGTCACCGGAGGCAATGCCGGAAGGACAACCTCCGGCCTCGTGTCCCTGAGGTCACCCTCACCCATCCCGT CACCAAATACATTATGACATGAGCGCTGACCTCGAGGTCGTGACAAGCACATGGGTCCTGGTCGTGGGACTGATGG CCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGCCTCTGGTGGCTGCAATACTTTCTGACAAGGGTCGCC ATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGA TCTGTCCATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGTTTTGCCGGAGTGGATG ATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATGCAGCTCCCCTGTGAGCCTGACCTGACGTCGCCGTCCTGACAA GCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGAGACTCCGTGACACCCATTGACACCACTATG GCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGATACGCTGCCCAAGGCTATAAGGT CCTGGTCCTGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGAGTGAGAAACTCCA TCCTACGGATTCCAATACTCCCCGGACAGAGAGTGGAGTTLCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGG ATTCTCCGACACAGCCGCTTGCGGAGACATTATCAATGCCTCCCCGTCAGCGCTAGGAGAGGGCAGAGAGATTCTGCTCG GCCCTGCCGATGGCCATGAGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGATGCC GAACTGATTGAGGCTAACCTCCTGTGGAACCCTGCCATTGCCTCCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCCT CACCACAAGCCAAACCCTCCTGTTTAACATTCTGGGACTGGTCCAGGCTTGGAAAAGCAAAAAGACACCCATGGGCTTTA CTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCCGTCTGGGCTAGGCCTGACTATATGTTTGCCCCTACCCTCTGGGC TAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTCAGCGTCATCCCTA CCTCCGGCGATGTGGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGATTGC CATAGCAAAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCT ALGTCCAGTATCTGTATAAGGGAAGGTGGGTGCCTGGCGCTGTGTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTG CTCCTGGCTCTGCCTCAGAGAGCCTATAGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTC CGGCGGAGCCTATGACATTATCATTTGCGATGAGTGTGCCAGAAGCGTCAGGGCTAGGCTCCTGGCTAGGGGAGGCAGAG CCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAAAAGGCTGTGGCTCACATTAACTCCGTGTGGAAG CGGCACAACCGATAGGTCCGGCGCTCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTCCCCGGATGCGTCC GATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCT  ${\tt CAGGGCTGTGGCTCTGGTCGCCTTTAAGATTATGTCCGGCGAAGTGCCTAGCACAGAGGATCTGGTCAACCTCC}$ TGCCTGCCATTCTGTCCTACGATACCAGATGCTTTGACTCCACCGTCACCGAAAGCGATATCAGAACCGAAGAGGCTATC TATCAGTGTTGCGATCTcGAcCCCCAAGAGCTCACCCCTGCCGAAACCACAGTGAGACCTGAGAGCCTATATGAATACCCC TGGCCTCCCGTCTGCCAAGACCATCTGGAgTTtTGGCCCCAACCCGAATACGATCTGGAACTGATTACCTCCTGCTCCA GCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTATCTGGGAAAGGTCATCGATACCCTCACCTGTGGC TTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGGCTCCCCTCGGCGAGCCGCTGCCATTCCCCTCGAGGTCATCAA AGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGCCAAACTGGTCGGCGGAGTGCTCG CCGCTCTGGCTGCCTATTGCCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCTTGC GAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGCCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGG AGACCCTGGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTT GGTTTTGCCTCCTGCTCAGCTCCAGCACAAGCGGAATCACAGGCGATAACACCACACACCACAGGCCTGCCCCTAGC CCTGTAACTGGACCAGAGGCGAAAGGTGTGACCTCGAGGATAGGGATGAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTG AATGTGAGAGGCGGAAGGGATGCCGTCATCCTCGTGATGTGCGTCGTGCATCCCACACTGGGAGTGAGAGCCACAAGGAA AACCTCCGAGAGAAGCCAACCCAGAGGCAGAAGGCAACCCATTCCCAAAGCCAGAAGGCCTGAGGGAAACGTCAGCGTCG CCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACACCCCTCGCCAGAGCCGCTTGGGAAAGC GAACCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGG AGACCCTATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATC TGACACCCCTCAGaGAcCCCTCCACCGAAGACCTCGTGAATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTC GCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAATgtcgactgagaattcgcc

### Cassette B

# 146/216

GCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGG ACTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAA ACGATTGCCCTGGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCC ACATGCATTAACGGAGTGTGTCCCGCTACCCAACTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTC CGCCCTCTACGTCGGCGATCTGTGTGGCTCCCACGCTCCCACAGGCTCCGGCAAAAGCACAAAGGTCCCCGCTGCCTATG CCGCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTCAGGACATGGGCTCAGCCTGGCTATCCCTGGCCCCTCTAC GGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCCACCGAAGACGTCGTGTGTTGCTCCATGTC CTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCAAAAGCTCCCCATTGCCCTCGACACAGAGGTCG TCCACCGGATTCACAAAGGTCTGCGGAGCCCCTCCCTGTGTGATTGGCGGAGCCGGAAACAATACCCTCCACTGTCCCAC AAGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTCCAAGTTTGGCTATGGCGCTAAGGATGTGAGAT GCCATGCCAGAATCTCCGGCATTCAGTATCTGGCTGGCCTCAGCACACTGCCTGGCAATCCCGCTATCGCTAGCCTCATG GCTTTCACAGCCGCTGTGACACAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCGGCGTCAGGGC TACCAGAAAGACAAGCGAAAGGTCCCAGCCTCTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCA ATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCATGAGAATCTGGAAACCACAATGAGAAGCCC TGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTCGCCACACCCCCTGGCTCCG TGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAACTGGTCTTC GATATCACAAAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGT CACCGCTGCCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAG TGCTCGCCGGATGCAATACCTGTGTGACACAGACAGTGGATTTCTCCCTcGAcCCCACATTCACAATCGAAACCACAACC CTCCCCAAGACGCTGTGTCCCACGGACCCACACCCCTCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACTGAC ACACCCTGTGACAAAGTATATCATGACCTGTGCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGAC CCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGATGCGTCATCGGAGGCGCTGGCAATAACACACTGCATTGC CCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGAACCTGTGGCTCCAGCGATCTGTATCTGGT CACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGGGGGGATAGCAGAGGCTCCCTGCTCAACATGTGGTCCGGCACAT TCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCCGCTCCCAATTACACATTCGCTCTGTGGCACTCCACC GATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTGCTCGCCAC ATACGTCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGAC TGCATCAGTGGAGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACACTG ACATGCGGATTCGCTGACCTCGCCCTGACCAAAGGCCTTACTGTTGGCATTACCCTCCCAAACCCTGTGGCATTGTGCC TGCCAAAAGCGTCTGCGGACCCGTCTACTGTGAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCG CCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACATACCAAGCCACAGTGTGTGCCAGAGCCCAAGCCCCTCCC CCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTCTGCGGAATCGTCCCCGCTAAGTCCGTGTG GATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGG ATGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAG CCGTCCAGAATCTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGGTCATC GCTCCCGCTGTGCAAACCAATTGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCA ATACCTCGCCGGACTGTCCACCCTCCCCGGACTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATG TGCCTGAGTCCGACGCTGCCGCTAGGGTCACCGCTATCCTCGCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGC GGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCATAGCTCCGTGCTCTGCGAATGCTATGACGC TGGCTGTGCCTGGTACGAACTGACACCCGCTGAGACAACCGTCAGGCTCAGGCTTACATGGGCTGGGTGGCTGCCCAAC ATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAA TAACGCTCTGTCCAACTCCCTGCTCAGGCATCACAATCTGGTCTACTCCACCACAAGCAGAAGCGCTTGCCAAAGGCAAA AGAAAGTGACAGCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGAC GTCAAGTTTCCCGGAGGCGGAAGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCTGGTCGCCTATCAGGCTACCGT ACAATACCAGACCCCTCTGGGAAACTGGTTCGGATGCACAGTGCCTCCCCCTAGGAAAAAGAGAACCGTCGTGCTCACC GAAAGCACACTGTCCACCGCTCTGGCTGAGCTCGCCACAAAGTCCTTCGGAAGCACAACCTCCAGGTCCGCCTGTCAGAG ACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTCGACCAAGCCGAAACCGCTG GTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCCGAGTTLTTTACCGAACTGGATGGCGT CCTGAAACTGACACCCATTGCCGCTGCCGGAAGGCTCGACCTCAGCGGATGGTTTACCGCTGGCTATAGCGGAGGCGATA TCTATCACTCCGCCTCCAGGCAAGCCGAAGTGATTGCCCCTGCCGTCCAGACAAACTGGCAGAAACTGGAAGTGTTTTGG GCTAAGCATATGTGGAACTTTTGCAGAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAA AGCCAGAGCCGCTTGCAGAGCCGCTGGCCTCTTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAG AGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTCGGCCCTCTGACAAACTCCAGGGGAGAGAATTGCGGATAC AGAAGGTGTAGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTCATCATGCACACAAGGTGTCACTGTGGCGC TGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGAGAGGTCAGCTTTAGGGTCG GCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCCAAGGAAGTG AAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGGCTTGCTCCCTGACACCCCCTCACTCCGCCAA AGGCAGAGACGCTGTGATTCTGCTCATGTGTGTGGTCCACCCTACCCTGTGTTTGACATTACCAAACTGCTCCTGGCTG TGTTTGGCCCTATGCTCACCGATCCCTCCACATTACCGCTGAGGCTGCCGGAAGGAGACTGGCTAGGGGAAGCCCTCCC TCCATGGCTAGCTCCAGCGCTAGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGC TGGCCATGCCGTCGGCATTTTCAGAGCCGCTGACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCGGAC CCGATCAGAGACCCTATTGCTGGCACTATCCCCCTAAGCCTAGGCATGTGGGACCCGGAGAGGGAGCCGTCCAGTGGATG AATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCTACCCATctcgagtgagaattcgcc

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Cassette C

qqcqqat ccaccat gctcqagTGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGAT TCTGAATGCCGCTAGCCTCGCCGGAACCCATATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAG AGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATGCTGATTCACCTCCACCAAAACATTGTGGATGTGCAATAC CTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTATGTGTCCCACGCTAGGCCTAGGTGGTTCTG GTTCTGTCTGCTCGCCGCTGGCGTCGGCATTTACCTCCTGCCTAACAGAGCCGCTGCCGCTACCCTCGGCTTTG GCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGAAGGGTCCAG GGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGA¹TTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGC TAGGAGATTCGCTCAGGCTCTGCCTGTGGGCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTG ACTATGAGCCTACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGACCGTCTACCATGGCGCTGGC ACAAGGACAATCGCTAGCCCTTGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTCGTGTTAGCCA AATGGAAACCAAACTGATTACCTGGGGCGCTAAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCG GCTGGCCCGCTCCCCAAGGCTCCAGGTCCCTGACACCCTGTAAGGTCGTGATTCTGGATAGCTTTTGACCCTCTGGTCGCC GAAGAGGATGAGAGAGAGATTAGCGTCCCCGCTGAGAATCTGAGAAAGTCCCTGACAGGCACATACGTCTACAATCACCT CCAAAGCCGTgGALTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAATGCCCTCGGC ATTAACGCTGTGGCTTACTATAGGGGACTGGATGTCCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGA TATGTCCGCCGATCTGGAAGTGGTCACCTCCACCTGGGTGCTCGTGGGAGGCGTCCTGGCTGCCCTCGCCGCTTACTGTC TGTCCACCGGAGCCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGCTAACACATGCGTCACCCAAACC GTqGAtTTTAGCCTCGACCCTAACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGG AGTGTATCTGCTCCCCAGAAGGGGACCCAGAAGGGCTCTGGCTCACGGAGTGAGAGTGCTCCGAGGATGGCGTCAACTATG CCACAGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTCAGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCAC GCTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAAACCCCTGGCGCTAAGCAAAACATTCAGCT GCCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTTGGCTAGCTGTAGGAGACTGACAGTGGTCCTG CGACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCTATCATTCAGAGACTGCATGGCCTCA GCGCTTTCTCCTGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTAC ACAAACGTGGALCAAGACCTCTACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTG TGAGTGTTACGATGCCGGATGCGCTTGGTATAGGTCCGAGCTCAGCCCTCTGCTCCTGTCCACCACACAGTGGCAGGTCC TGCCTTGCTCCTTCACAACCCTCCCGCTCTGTCCACCGGACTGAGAAAGCTCGGCGTCCCCCTCTGAGAGCCTGGAGG CATAGGGCTAGGTCGTGAGAGCCAGACTGCTCGCCAGAGGGGGGAAGGGCTAGCCCTCTGACAACCTCCCAGACACTGCT CTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCTCTGTGGATLCTCCAGGCTA GCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATGGTGAAAAAAC GGAACCATGAGGATTGŤGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGG AGAGGTCGCCCTCAGCACAACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGAC TCCTGGCTCGGCAATATCATTAGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTATGTGAC CCCCTCCCAGAAAGAAAAGGACAGTGGTCCTGACAGAGTCCACCCTCAGCACAGCCCCTCGCCGAACTGGCTACCAAAAGC TTTGGCTCCAGCTCCACCTCCGGCATTACCGGAGACAATACCACAACCTCCGTGTCCTGCCAAAGGGGATACAAAGGCGT CTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGGAGCCGAAATCACAGGCCATGTGTTTTCTGGTCGGCCAAC TGTTTACCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTATCCCGGACACATTTTCGTCGGC GCTGGCCTCGCCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCGG AGACATTTGGGATTGGATTTGCGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCAAACTGATGCCCCAACTGCCTG GCATTCCCTTTAACTCCAGCATTGTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGG GAAGGCAATGCCTCCAGGTGTAGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGG ATGGGGACCCATTAGCTATGCCAATGGCTCCAGGACAGAGGAAGCCATTTACCAATGCTGTGACCTCGACCCTCAGGCTA GGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGAGTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACAGCC TATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACATTCTTTAGCGTCCTGATTGCCAGAGACCA AGTTTTTCACAGAGCTCGACGGAGTGAGACTGCATAGGTTTGCCCCTCCTGTAAGCCTCTGCTCAGGGAAACCTGTTAC ATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCTGCGGAGACGATCTGGTCGTGAT TATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTC CTCAGCACAACCCAATGGCAAACCGGACACAGAATGGCTTGGGATATGATGATGAATTGGTCCCCCACAGCCGCTCTGGT CATGGCTCAGCTCCTGAGAATCCCTCAGGCTCCCGGAGCCCTCGTGGTCGGCGTGTGTGCCGCTATCCTCAGGAGAC ACGTCGGCCCTGGCGAAGGCGCTGTGCAATGGATGAACAGACACGATAGCCCTGACGCTGAGCTCATCGAAGCCAATCTG CTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAATGAGGGAGTGTTTACCGGACTGACACACAT TGACGCTCACTTTCTGTCCCAGACAAAGCAAAGCGGAGAGATTTCCCTTACCTCGTGGCTAGGGGAAGGAGACAGCCTA TCCCTAAGGCTAGGAGACCCGAAGCCAGACCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAATCTGATTGTG TTTCCCGATCTGGGAGTGAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCCTCGCCGTCATGGG ATACGCTACCGGAAACCTCCCCGGATGCTCCTTCTCCATCTTTCTGCTCGCCCTCTCTCCTGCCTCACCGTCCCCGCTA AAAATCATGAGCGGAGAGGTCAGCTATAGCTCCATGCCTCCCCTCGAGGGAGAGCCTGGCGATCCCGATCTGTCCGACGG AAGCTGGAGCACAGTGTCCAGCGAAGCCGGAAGGCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAAGCGAAAACAAAG TGGTCATCCTCGACTCCTTCGATCCCCTCGTGGCTGAGGAAGTGGGATGGCCTGCCCCTCAGGGAAGCAGAAGCCTCACC  ${\tt CCTTGCACATGCGGAAGCTCCGACCTCTACCTCGTGACAAGGCATGCCGATGCTGTAGCGGAGGCGCTTACGATATCAT}$ TATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTCACCTTTACCATTGAGACAA  ${\tt CCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGAGGCAGAACCGGAAGGGGAAAGCCTGGCATTGACTGTTTC}$ A GAAAG CATCCCGAAG CCACATACT CCAGGTGTGGCT CCGGCCCTTGGATTACCCCTAGGTGTCTGGTgGAŁTATCCCTAGGTGTCTGGTTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGGALTATCCCTAGGTGTGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCAGAATCTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCCGCCCTCGTGACACCCTGTGCCGCTGAGGAACAGA

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AACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCATAACCTCGTGTATATCTCCAGCGAATGCACAACCCCT TGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGATCTGTGAGGGTCCTGTCCGACTTTAAGACATGGCTCAAGGCTAA GCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGCTTATAAGGGAGTGTGGAGGGGAGACGGAAGCG GACCCTGGATCACACCCACATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTATACCATT TTCAAAagatctTGAgtcgacgaattcgcc

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# Melanoma Savine design

Two savines - one containing scrambled melanocyte differentiation Ags
- one containing scrambled melanoma cancer specific Ags

Genes in melanocyte differentiation Savine

### ap100

MDLVLKRCLLHLAVIGALLAVGATKVPRNQDWLGVSRQLRTKAWNRQLYPEWTEAQRLDCWRGGQVSLKVSNDGPTLI GANASFSIALNFPGSQKVLPDGQVIWVNNTIINGSQVWGGQPVYPQETDDACIFPDGGPCPSGSWSQKRSFVYVWKTW GQYWQVLGGPVSGLSIGTGRAMLGTHTMEVTVYHRRGSRSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLR NQPLTFALQLHDPSGYLAEADLSYTWDFGDSSGTLISRALVVTHTYLEPGPVTAQVVLQAAIPLTSCGSSPVPGTTDG HRPTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEVISTAPVQMPTAESTGMTPEKVPVSEVMGTTLA EMSTPEATGMTPAEVSIVVLSGTTAAQVTTTEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVK RQVPLDCVLYRYGSFSVTLDIVQGIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMEISSPGCQPPAQRLCQPVLP SPACQLVLHQILKGGSGTYCLNVSLADTNSLAVVSTQLIMPGQEAGLGQVPLIVGILLVLMAVVLASLIYRRRLMKQD FSVPQLPHSSSHWLRLPRIFCSCPIGENSPLLSGQQV

### MART

MPREDAHFIYGYPKKGHGHSYTTAEEAAGIGILTVILGVLLLIGCWYCRRNGYRALMDKSLHVGTQCALTRRCPQEGFDHRDSKVSLQEKNCEPVVPNAPPAYEKLSAEQSPPPYSP

### TRP-1

PAFLTWHRYHLLRLEKDMQEMLQEPSFSLPYWNFATGKNVCDICTDDLMGSRSNFDSTLISPNSVFSQWRVVCDSLED YDTLGTLCNSTEDGPIRRNPAGNVARPMVQRLPEPQDVAQCLEVGLFDTPPFYSNSTNSFRNTVEGYSDPTGKYDPAV RSLHNLAHLFLNGTGGQTHLSSQDPIFVLLHTFTDAVFDEWLRRYNADISTFPLENAPIGHNRQYNMVPFWPPVTNTE MFVTAPDNLGYTYE

### Tyros

MLLAVLYCLLWSFQTSAGHFPRACVSSKNLMEKECCPPWSGDRSPCGQLSGRGSCQNILLSNAPLGPQFPFTGVDDRE SWPSVFYNRTCQCSGNFMGFNCGNCKFGFWGPNCTERRLLVRRNIFDLSAPEKDKFFAYLTLAKHTISSDYVIPIGTY GQMKNGSTPMFNDINIYDLFVWMHYYVSMDALLGGSEIWRDIDFAHEAPAFLPWHRLFLLRWEQEIQKLTGDENFTIP YWDWRDAEKCDICTDEYMGGQHPTNPNLLSPASFFSSWQIVCSRLEEYNSHQSLCNGTPEGPLRRNPGNHDKSRTPRL PSSADVEFCLSLTQYESGSMDKAANFSFRNTLEGFASPLTGIADASQSSMHNALHIYMNGTMSQVQGSANDPIFLLHH AFVDSIFEQWLQRHRPLQEVYPEANAPIGHNRESYMVPFIPLYRNGDFFISSKDLGYDYSYLQDSDPDSFQDYIKSYL EQASRIWSWLLGAAMVGAVLTALLAGLVSLLCRHKRKQLPEEKQPLLMEKEDYHSLYQSHL

### TRP2

MSPLWWGFLLSCLGCKILPGAQGQFPRVCMTVDSLVNKECCPRLGAESANVCGSQQGRGQCTEVRADTRPWSGPYILR NQDDRELWPRKFFHRTCKCTGNFAGYNCGDCKFGWTGPNCERKKPPVIRQNIHSLSPQEREQFLGALDLAKKRVHPDY VITTQHWLGLLGPNGTQPQFANCSVYDFFVWLHYYSVRDTLLGPGRPYRAIDFSHQGPAFVTWHRYHLLCLERDLQRL IGNESFALPYWNFATGRNECDVCTDQLFGAARPDDPTLISRNSRFSSWETVCDSLDDYNHLVTLCNGTYEGLLRRNQM GRNSMKLPTLKDIRDCLSLQKFDNPPFFQNSTFSFRNALEGFDKADGTLDSQVMSLHNLVHSFLNGTNALPHSAANDP IFVVLHSFTDAIFDEWMKRFNPPADAWPQELAPIGHNRMYNMVPFFPPVTNEELFLTSDQLGYSYAIDLPVSVEETPG WPTTLLVVMGTLVALVGLFVLLAFLQYRRLRKGYTPLMETHLSSKRYTEEA

### MC1R

MAVQGSQRRLLGSLNSTPTAIPQLGLAANQTGARCLEVSISDGLFLSLGLVSLVENALVVATIAKNRNLHSPMYCFIC CLALSDLLVSGTNVLETAVILLLEAGALVARAAVLQQLDNVIDVITCSSMLSSLCFLGAIAVDRYISIFYALRYHSIV TLPRAPRAVAAIWVASVVFSTLFIAYYDHVAVLLCLVVFFLAMLVLMAVLYVHMLARACQHAQGIARLHKRQRPVHQG FGLKGAVTLTILLGIFFLCWGPFFLHLTLIVLCPEHPTCGCIFKNFNLFLALIICNAIIDPLIYAFHSQELRRTLKEV LTCSW

### MUC1F

 ${\tt MTPGTQSPFFLLLLLTVLTVVTGSGHASSTPGGEKETSATQRSSVPSSTEKNAVSMTSSVLSSHSPGSGSSTTQGQDV\\ {\tt TLAPATEPASGSAATWGQDVTSVPVTRPALGSTTPPAHDVTSAPDNK}$ 

Figure 27



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### MUC1R

NRPALGSTAPPVHNVTSASGSASGSASTLVHNGTSARATTTPASKSTPFSIPSHHSDTPTTLASHSTKTDASSTHHSS VPPLTSSNHSTSPQLSTGVSFFFLSFHISNLQFNSSLEDPSTDYYQELQRDISEMFLQIYKQGGFLGLSNIKFRPGSV VVQLTLAFREGTINVHDVETQFNQYKTEAASRYNLTISDVSVSDVPFPFSAQSGAGVPGWGIALLVLVCVLVALAIVY LIALAVCQCRRKNYGQLDIFPARDTYHPMSEYPTYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLSYTNPAVAAASANL

NB Muc 1 Repeat sequences in the middle of the gene were removed

Genes in melanoma specific Savine

BÁGE

 ${\tt MAARAVFLALSAQLLQARLMKEESPVVSWRLEPEDGTALCFIF}$ 

### GAGE - 1

 ${\tt MSWRGRSTYRPRPRRYVEPPEMIGPMRPEQFSDEVEPATPEEGEPATQRQDPAAAQEGEDEGASAGQGPKPEADSQEQGPMPQTGCECEDGPDGQEMDPPNPEEVKTPEEEMRSHYVAQTGILWLLMNNCFLNLSPRKP}$ 

gp100In4

SWSQKRSFVYVWKTWGEGLPSQPIIHTCVYFFLPDHLSFGRPFHLNFCDFL

### MAGE-1

MSLEQRSLHCKPEEALEAQQEALGLVCVQAATSSSSPLVLGTLEEVPTAGSTDPPQSPQGASAFPTTINFTRQRQPSE GSSSREEEGPSTSCILESLFRAVITKKVADLVGFLLLKYRAREPVTKAEMLESVIKNYKHCFPEIFGKASESLQLVFG IDVKEADPTGHSYVLVTCLGLSYDGLLGDNQIMPKTGFLIIVLVMIAMEGGHAPEEEIWEELSVMEVYDGREHSAYGE PRKLLTODLVOEKYLEYROVPDSDPARYEFLWGPRALAETSYVKVLEYVIKVSARVRFFFPSLREAALREEEEGV

### MAGE-3

MPLEQRSQHCKPEEGLEARGEALGLVGAQAPATEEQEAASSSSTLVEVTLGEVPAAESPDPPQSPQGASSLPTTMNYP LWSQSYEDSSNQEEEGPSTFPDLESEFQAALSRKVAELVHFLLLKYRAREPVTKAEMLGSVVGNWQYFFPVIFSKASS SLQLVFGIELMEVDPIGHLYIFATCLGLSYDGLLGDNQIMPKAGLLIIVLAIIAREGDCAPEEKIWEELSVLEVFEGR EDSILGDPKKLLTQHFVQENYLEYRQVPGSDPACYEFLWGPRALVETSYVKVLHHMVKISGGPHISYPPLHEWVLREG EE

### PRAME

MERRRLWGSIQSRYISMSVWTSPRRLVELAGQSLLKDEALAIAALELLPRELFPPLFMAAFDGRHSQTLKAMVQAWPF
TCLPLGVLMKGQHLHLETFKAVLDGLDVLLAQEVRPRRWKLQVLDLRKNSHQDFWTVWSGNRASLYSFPEPEAAQPMT
KKRKVDGLSTEAEQPFIPVEVLVDLFLKEGACDELFSYLIEKVKRKKNVLRLCCKKLKIFAMPMQDIKMILKMVQLDS
IEDLEVTCTWKLPTLAKFSPYLGQMINLRRLLLSHIHASSYISPEKEEQYIAQFTSQFLSLQCLQALYVDSLFFLRGR
LDQLLRHVMNPLETLSITNCRLSEGDVMHLSQSPSVSQLSVLSLSGVMLTDVSPEPLQALLERASATLQDLVFDECGI
TDDQLLALLPSLSHCSQLTTLSFYGNSISISALQSLLQHLIGLSNLTHVLYPVPLESYEDIHGTLHLERLAYLHARLR
ELLCELGRPSMVWLSANPCPHCGDRTFYDPEPILCPCFMPN

### TRP2 IN2

LMETHLSSKRYTEEAGGFFPWLKVYYYRFVIGLRVWQWEVISCKLIKRATTRQP

### NYNS01a

MQAEGRGTGGSTGDADGPGGPGIPDGPGGNAGGPGEAGATGGRGPRGAGAARASGPGGGAPRGPHGGAASGLNGCCRC GARGPESRLLEFYLAMPFATPMEAELARRSLAQDAPPLPVPGVLLKEFTVSGNILTIRLTAADHRQLQLSISSCLQQL SLLMWITQCFLPVFLAQPPSGQRR

### NYNSO1b

MLMAQEALAFLMAQGAMLAAQERRVPRAAEVPGAQGQQGPRGREEAPRGVRMAARLQG

LAGE1

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 $\label{thm:local-possible} $$ \mathbf{MQAEGQGTGGSTGDADGPGGGGIPDGPGGGAAGGPGEAGATGGRGPRGAGAARASGPRGGAPRGPHGGAASAQDGRCPC} $$ \mathbf{GARRPDSRLLQLHITMPFSSPMEAELVRRILSRDAAPLPRPGAVLKDFTVSGNLLFIRLTAADHRQLQLSISSCLQQLSLLMWITQCFLPVFLAQAPSGQRR} $$$ 

```
Differentiation Savine Scramble process
              : melanoma
Input filename
              : Diffmucg.txt
Output filename : Diffmucs.txt
Number genes
Number segments : 187
Segment length : 30
Segment overlap : 15
Segments in original order:
        : gp100
Segment#
Offset
       : 1
1st Codon : 1
AAM D L V L K R C L L H L A V I G A L L A V G A T K V P R
GCCGCTATGGATCTGGTCCTGAAAAGGTGTCTGCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGA
Gene
        : gp100
Segment# : 2
        : 16
Offset
1st Codon : 1
V I G A L L A V G A T K V P R N Q D W L G V S R Q L R T K A
GTGATTGGCGCCTCTGCCCGCCGCGCCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT
Gene
        : gp100
Segment#
Offset
        : 31
1st Codon: 1
N Q D W L G V S R Q L R T K A W N R Q L Y P E W T E A Q R L
: gp100
1st Codon : 1
W N R O L Y P E W T E A Q R L D C W R G G Q V S L K V S N D
TGGAATAGGCAACTGTATCCCGAATGGACAGAGGCTCAGAGACTGGATTGCTGGAGGGGAGGCCAAGTGTCCCTGAAAGTGTCCCAACGAT
        : gp100
Gene
Segment# : 5
Offset
1st Codon : 1
D C W R G G Q V S L K V S N D G P T L I G A N A S F S I A L
GACTGTTGGAGAGGCGGACAGGTCAGCCTCAAGGTCAGCAATGACGGACCCACACTGATTGGCGCTAACGCTAGCTTTAGCATTGCCCTC
        : gp100
Gene
Segment#
Offset
1st Codon: 1
GPTLIGANAS FSIALN FPGSQKVLPDGQVI
GGCCCTACCCTCATCGGAGCCAATGCCTCCTTCTCCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATT
        : gp100
Gene
Segment# : 7
Offset : 91
N F P G S Q K V L P D G Q V I W V N N T I I N G S Q V W G G
AACTTTCCCGGAAGCCAAAAGGTCCTGCCTGACGGACAGGTCATCTGGGTGAATAACACAATCATTAACGGAAGCCAAGTGTGGGGCGGA
        : gp100
Segment# : 8
Offset
        : 106
1st Codon : 1
```

Figure 27 (Cont)

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W V N N T ·I I N G S Q V W G G Q P V Y P Q E T D D A C I F P TGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGGAGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCT : gp100 Segment# : 9 Offset : 121 1st Codon : 1 Q P V Y P Q E T D D A C I F P D G G P C P S G S W S Q K R S CAGCCTGTGTATCCCCAAGAGACAGACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCGGCTCCTGGTCCCAGAAAAGGTCC : gp100 Segment# : 10 Offset : 136 1st Codon : 1 D G G P C P S G S W S Q K R S F V Y V W K T W G Q Y W Q V L GACGGAGGCCCTTGCCCTAGCGGAAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTAGGAAGACATGGGGACAGTATTGGCAAGTGCTC Gene : gp100 Segment# : 11 Offset : 151 1st Codon : 1 F V Y V W K T W G Q Y W Q V L G G P V S G L S I G T G R A M TTCGTCTACGTCTGGAAAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGCAGAGCCATG Gene : gp100 Segment# : 12 Offset : 166 1st Codon : 1 G G P V S G L S I G T G R A M L G T H T M E V T V Y H R R G : gp100 Segment# : 13 : 181 1st Codon: 1 LGTHTMEVTVYHRRGSRSYVPLAHSSSAFT  $\tt CTGGGAACCCATACCATGGAGGTCACCGTCTACCATAGGAGGGCTCCAGGGTCCTACGTCCCCCTCGCCCATAGCTCCAGCGCTTTCACA$ Gene : gp100 Segment# : 14 Offset : 196 lst Codon : 1 S R S Y V P L A H S S S A F T I T D Q V P F S V S V S Q L R AGCAGAAGCTATGTGCCTCTGGCTCACTCCAGCTCCGCCTTTACCATTACCGATCAGGTCCCCTTTAGCGTCAGCGTCAGCCAACTGAGA : gp100 Segment# : 15 : 211 Offset 1st Codon : 1 I T D Q V P F S V S V S Q L R A L D G G N K H F L R N Q P L Gene : gp100 Segment# : 16 Offset : 226 1st Codon : 1 A L D G G N K H F L R N Q P L T F A L Q L H D P S G Y L A E GCCCTCGACGGAGGCAATAAGCATTTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCTAGCGGATACCTCGCCGAA Gene : gp100 Segment# : 17 Offset : 241 1st Codon : 1 FALQLHDPSGYLAEADLSYTWDFGDSSGT ACCTTTGCCCTCCAGCTCCACGATCCCTCCGGCTATCTGGCTGAGGCTGACCTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACA Gene : gp100 Segment# : 18 : 256 A D L S Y T W D F G D S S G T L I S R A L V V T H T Y L E P 

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```
: gp100
  Segment# : 19
                              : 271
  1st Codon : 1
    LISRALVVTHTYLEPGPVTAQVVLQAAIPL
  CTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGCTCAGGTCGTGCTCCAGGCTGCCATTCCCCTC
                             : gp100
 Segment# : 20
                            : 286
1st Codon: 1
G P V T A Q V V L Q A A I P L T S C G S S P V P G T T D G H
GGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTGTGCCAGCCCAACCGATGGCCAT
 Segment# : 21
                           : 301
    \texttt{T} \;\; \texttt{S} \;\; \texttt{C} \;\; \texttt{G} \;\; \texttt{S} \;\; \texttt{S} \;\; \texttt{P} \;\; \texttt{V} \;\; \texttt{P} \;\; \texttt{G} \;\; \texttt{T} \;\; \texttt{T} \;\; \texttt{D} \;\; \texttt{G} \;\; \texttt{H} \;\; \texttt{R} \;\; \texttt{P} \;\; \texttt{T} \;\; \texttt{A} \;\; \texttt{E} \;\; \texttt{A} \;\; \texttt{P} \;\; \texttt{N} \;\; \texttt{T} \;\; \texttt{A} \;\; \texttt{G} \;\; \texttt{Q} \;\; \texttt{V} \;\; \texttt{P} \;\; \texttt{A} \;\; \texttt{A} \;\; \texttt{P} \;\; \texttt{N} \;\; \texttt{A} \;\; \texttt{P} \;\; \texttt{N} \;\; \texttt{A} \;\; \texttt{A} \;\; \texttt{P} \;\; \texttt{N} \;\; \texttt{A} \;\; \texttt{P} \;\; \texttt{N} \;\; \texttt{A} \;\; \texttt{A} \;\; \texttt{P} \;\; \texttt{N} \;\; \texttt{A} \;\; \texttt{A
 ACCTCCTGCGGAAGCTCCCCGGTCCCCGGAACCACAGACGGACACAGACCCACAGCCGAAGCCCTAACACAACCGCTGGCCAAGTGCCT
                             : gp100
 Segment# : 22
Offset
                           : 316
1st Codon : 1
R P T A E A P N T T A G Q V P T T E V V G T T P G Q A P T
AGGCTTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACAACCCTGGCCAAGCCCCTACCGCT
Gene : gp100
Segment# : 23
Offset
                          : 331
Offset
1st Codon : 1
   T T E V V G T T P G Q A P T A E P S G T T S V Q V P T T E V
ACCACAGAGGTCGTGGGAACCACACCCGGACAGGCTCCCACAGCCGAACCCTCCGGCACAACCTCCGTGCAAGTGCCTACCACAGAGGTC
                            : gp100
Segment# : 24
                           : 346
1st Codon : 1  \hbox{ E P S G T T S V Q V P T T E V I S T A P V Q M P T A E S T G } 
GAGCCTAGCGGAACCACAAGCGTCCAGGTCCCACAACCGAAGTGATTAGCACAGCCCCTGTGCAAATGCCTACCGCTGAGTCCACCGGA
                            : gp100
Segment# : 25
Offset
                           : 361
1st Codon: 1
ISTAPVQMPTAESTGMTPEKVPVSEVMGTT
ATCTCCACCGCTCCCGTCCAGATGCCCACAGCCGAAAGCACAGGCATGACCCCTGAGAAAGTGCCTGTGTCCGAGGTCATGGGAACCACA
                            : gp100
Gene
Segment# : 26
Offset : 376
1st Codon : 1
  M T P E K V P V S E V M G T T L A E M S T P E A T G M T P A
ATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGATGGGCACAACCCTCGCCGAAATGTCCACCCTGAGGCTACCGGAATGACACCCGCT
                            : gp100
Segment# : 27
Offset
                           : 391
1st Codon : 1
  L A E M S T P E A T G M T P A E V S I V V L S G T T A A Q V
CTGGCTGAGATGAGCACACCCGAAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTC
Gene
                           : gp100
Segment# : 28
                          : 406
1st Codon : 1
E V S I V V L S G T T A A Q V T T T E W V E T T A R E L P I
Gene
                           : gp100
```

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```
Segment#
       : 29
Offset
        : 421
1st Codon : 1
 T T E W V E T T A R E L P I P E P E G P D A S S I M S T E
ACCACAACCGAATGGGTCGAGACAACCGCTAGGGAACTGCCTATCCCTGAGCCTGAGGGACCCGATGCCTCCAGCATTATGTCCACCGAA
Gene
        : qp100
       : 30
Segment#
       : 436
Offset
1st Codon : 1
 PEPEGPDASSIMSTESITGSLGPLLDGTAT
: qp100
Gene
Segment# : 31
Offset
       : 451
1st Codon : 1
 S I T G S L G P L L D G T A T L R L V K R Q V P L D C V L Y
AGCATTACCGGAAGCCTCGGCCCTCTGGTCGACGGAACCGCTACCCTCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCGTCCTGTAT
Gene
        : gp100
Segment# : 32
        : 466
1st Codon: 1
LRLVKRQVPLDCVLYRYGSFSVTLDIVQGI
CTGAGACTGGTCAAGAGACAGGTCCCCCTGACTGTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATT
Gene
        : gp100
Segment#
       : 33
Offset
        : 481
1st Codon: 1
RYGSFSVTLDIVQGIESAEILQAVPSGEGD
AGGTATGGCTCCTTCTCCGTGACACTGGATATCGTCCAGGGAATCGAAAGCGCTGAGATTCTGCAAGCCGTCCCCTCCGGCGAAGGCGAT
        : qp100
Segment# : 34
Offset
        : 496
1st Codon : 1
\begin{smallmatrix} E & S & A & E & I & L & Q & A & V & P & S & G & E & G & D & A & F & E & L & T & .V & S & C & Q & G & L & P & K & E \\ \end{smallmatrix}
GAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAA
Segment# : 35
Offset
       : 511
1st Codon : 1
A F E L T V S C Q G G L P K E A C M E I S S P G C Q P P A Q
GCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGCTTGCATGGAGATTAGCTCCCCGGGATGCCAACCCCCTGCCCAA
        : qp100
Gene
Segment#
       : 36
       : 526
Offset
1st Codon : 1
A C M E I S S P G C Q P P A Q R L C Q P V L P S P A C Q L V
: gp100
Gene
Segment# : 37
R L C Q P V L P S P A C Q L V L H Q I L K G G S G T Y C L N
AGGCTCTGCCAACCCGTCCTGCCTAGCCCTGCCTGTCAGCTCGTGCTCCACCAAATCCTCAAGGGAGGCTCCGGCACATACTGTCTGAAT
        : gp100
Segment# : 38
Offset
       : 556
1st Codon: 1
L H O I L K G G S G T Y C L N V S L A D T N S L A V V S T Q
CTGCATCAGATTCTGAAAGGCGGAAGCGGAACCTATTGCCTCAACGTCAGCCTCGCCGATACCAATAGCCTCGCCGTCGTCCACCCAA
Gene
        : gp100
Segment# : 39
        : 571
Offset
```

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```
1st Codon: 1
V S L A D T N S L A V V S T Q L I M P G Q E A G L G Q V P L
GTGTCCCTGGCTGACACAAACTCCCTGGCTGTGGTCAGCACACAGCTCATCATGCCCGGACAGGAAGCCGGACTGGGACAGGTCCCCCTC
Gene
         : gp100
Segment# : 40
Offset
         : 586
1st Codon: 1
L I M P G Q E A G L G Q V P L I V G I L L V L M A V V L A S
CTGATTATGCCTGGCCAAGAGGCTGGCCTCGGCCAAGTGCCTCTGATTGTGGGAATCCTCCTGGTCCTGATGGCCGTCGTCCTCCC
Gene
         : gp100
Segment# : 41
Offset
        : 601
1st Codon: 1
I V G I L V L M A V V L A S L I Y R R R L M K Q D F S V P
ATCGTCGGCATTCTGCTCGTGCTCATGGCTGTGGTCCTGGCTAGCCTCATCTATAGGAGAAGGCTCATGAAACAGGATTTCTCCGTGCCT
Gene : gp100
Segment# : 42
Offset
        : 616
Offset
1st Codon: 1
LIYRRRLMKQDFSVPQLPHSSSHWLRLPRI
CTGATTTACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCACTCCAGCTCCCACTGGCTGAGACTGCCTAGGATT
Gene
         : qp100
Segment# : 43
Offset
1st Codon : 1
Q L P H S S S H W L R L P R I F C S C P I G E N S P L L S G CAGCTCCCCCATAGCTCCAGCCATTGGCTCAGGCTCCCCAGAATCTTTTGCTCCTGCCCTATCGGAGAGAATAGCCCTCTGCTCAGCGGA
         : gp100
Segment# : 44
Offset
        : 646 🗸 '
1st Codon : 1
F C S C P I G E N S P L L S G Q Q V A A
TTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCT
Gene
        : MART
Segment# : 1
Offset
1st Codon: 1
A A M P R E D A H F I Y G Y P K K G H G H S Y T T A E E A A
: MART
Gene
Segment# : 2
Offset
K K G H G H S Y T T A E E A A G I G I L T V I L G V L L I
{\tt AAGAAAGGCCATGGCCATAGCTATACCACAGCCGAAGAGGCTGCCGGAATCGGAATCCTCACCGTCATCCTCGGCGTCCTGCTCCTGATT}
Gene : MART
Segment# : 3
Offset : 31
1st Codon : 1
G I G I L T V I L G V L L I G C W Y C R R N G Y R A L M
GGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTGCTCATCGGATGCTGGTACTGTAGGAGAAGGAATGGCTATAGGGCTCTGATG
Gene
        : MART
Segment# : 4
Offset
1st Codon: 1
G C W Y C R R R N G Y R A L M D K S L H V G T Q C A L T R R
GGCTGTTGGTATTGCAGAAGGAGAAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGA
        : MART
Gene
Segment# : 5
Offset : 61
1st Codon : 1
DKSLHVGTQCALTRRCPQEGFDHRDSKVSL
```

Figure 27 (Cont)

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```
{\tt GACAAAAGCCTCCACGTCGGCACACAGTGTGCCCTCACCAGAAGGTGTCCCCCAAGAGGGATTCGATCACAGAGACTCCAAGGTCAGCCTC}
       : MART
Gene
Segment#
      : 6
       : 76
Offset
1st Codon : 1
 C P O E G F D H R D S K V S L Q E K N C E P V V P N A P P A
TGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTCCCCAATGCCCCTCCCGCT
Gene
       : MART
Segment# : 7
Offset
1st Codon : 1
 O E K N C E P V V P N A P P A Y E K L S A E Q S P F P Y S P
: MART
Gene
Segment# : 8
       : 106
Offset
1st Codon : 1
Y E K L S A E Q S P P P Y S P A A
TACGAAAAGCTCAGCGCTGAGCAAAGCCCTCCCCCTTACTCCCCCGCTGCC
       : TRP-1
Segment# : 1
1st Codon : 1
AAPAFLTWHRYHLLRLEKDMQEMLQEPS,FS
GCCGCTCCCGCTTTCCTCACCTGGCACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTCCTTCTCC
       : TRP-1
Gene
Segment# : 2
Offset
       : 16
1st Codon : 1
LEKDMQEML QEPSFSLPYWN FATGKN V CDI
: TRP-1
Gene
Segment# : 3
Offset
       : 31
L P Y W N F A T G K N V C D I C T D D L M G S R S N F D S T
CTGCCTTACTGGAACTTTGCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACA
       : TRP-1
Gene
Segment# : 4
Offset
      : 46
C T D D L M G S R S N F D S T L I S P N S V F S Q W R V V C
TGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCCAATAGCGTCTTCTCCCCAGTGGAGGGTCGTGTGT
       : TRP-1
Gene
Segment#
      : 5
Offset
       : 61
1st Codon : 1
LISPNSVFSQWRVVCDSLEDYDTLGTLCNS
CTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGATAGCCTCGAGGATTACGATACCCTCGGCACACTGTGTAACTCC
       : TRP-1
Gene
Segment# : 6
D S L E D Y D T L G T L C N S T E D G P I R R N P A G N V A
GACTCCCTGGAAGACTATGACACACTGGGAACCCTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCT
       : TRP-1
Segment# : 7
Offset
       : 91
TEDGPIRRNPAGNVARPMVQRLPEPQDVAQ
ACCGAAGACCCATTAGGAGAAACCCTGCCGGAAACGTCGCCAGACCCATGGTGCAAAGGCTCCCCGAACCCCAAGACGTCGCCCAA
```

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        : TRP-1
Segment# : 8
Offset
        : 106
1st Codon : 1
R P M V Q R L P E P Q D V A Q C L E V G L F D T P P F Y S N AGGCCTATGGTCCAGAGACTGCCTGAGCCTCAGGATGTGGCTCAGTGTCTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAAT
        : TRP-1
Segment# : 9
 C L E V G L F D T P P F Y S N S T N S F R N T V E G Y S D P
{\tt TGCCTCGAGGTCGGCCTCTTCGATACCCCTCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCT}
        : TRP-1
Segment# : 10
        : 136
1st Codon: 1
S T N S F R N T V E G Y S D P T G K Y D P A V R S L H N L A
AGCACAAACTCCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCT
Gene : TRP-1
Segment# : 11
Offset
       : 151
1st Codon : 1
T G K Y D P A V R S L H N L A H L F L N G T G G Q T H L S S
: TRP-1
Gene
Segment# : 12
Offset
1st Codon : 1
H L F L N G T G G Q T H L S S Q D P I F V L L H T F T D A V
Segment# : 13
Offset
       : 181
lst Codon: 1
QDPIFVLLHTFTDAVFDEWLRRYNADISTF
CAGGATCCCATTTTCGTCCTGCTCCACACATTCACAGACGCTGTGTTTGACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTT
Gene
       : TRP-1
Segment# : 14
Offset : 196
1st Codon : 1
F D E W L R R Y N A D I S T F P L E N A P I G H N R Q Y N M
: TRP-1
Gene
Segment# : 15
       : 211
Offset
1st Codon : 1
PLENAPIGHNR QYNM VPFWPPVTNTEMFVT
CCCCTCGAGAATGCCCCTATCGGACACAATAGGCAATACAATATGGTCCCCTTTTGGCCTCCCGTCACCAATACCGAAATGTTTTGTGACA
Gene
       : TRP-1
Segment# : 16
Offset : 226
1st Codon: 1
V P F W P P V T N T E M F V T A P D N L G Y T Y E A A
GTGCCTTTCTGGCCCCCTGTGACAAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATGAGGCTGCC
       : Tyros
Segment# : 1
Offset
A A M L L A V L Y C L L W S F Q T S A G H F P R A C V S S K
{\tt GCCGCTATGCTCCTGGCTGTGCTCTACTGTCTGCTCTGGTCCTTCCAAACCTCCGCCGGACACTTTCCCAGAGCCTGTGTCTCCAGCAAA}
Gene
Segment# : 2
```

Figure 27 (Cont)

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Offset Q T S A G H F P R A C V S S K N L M E K E C C P P W S G D R : Tyros Segment# : 3 Offset : 31 1st Codon : 1 N L M E K E C C P P W S G D R S P C G Q L S G R G S C Q N I AACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGCTCCTGCCAAAACATT : Tyros Gene Segment# : 4 : 46 Offset 1st Codon : 1 S P C G Q L S G R G S C Q N I L L S N A P L G P Q F P F T G AGCCCTTGCGGACAGCTCAGCGGAAGGGGAAGCTGTCAGAATATCCTCCTGTCCAACGCTCCCTCGGCCCTCAGTTTCCCTTTACCGGA Gene : Tyros Segment# : 5 Offset 1st Codon : 1 L S N A P L G P Q F P F T G V D D R E S W P S V F Y N R T Gene : Tyros : 6 Segment# Offset 1st Codon : 1 V D D R E S W P S V F Y N R T C Q C S G N F M G F N C G N C GTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAACTGT : Tyros Segment# : 7 : 91 Offset 1st Codon : 1 CQCSGNFMGFNCGNCKFGFWGPNCTERRLL TGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATTCGGATTCTGGGGCCCTAACTGTACCGAAAGGAGACTGCTC : Tyros Gene Segment# : 8 : 106 Offset 1st Codon : 1 K F G F W G P N C T E R R L L V R R N I F D L S A P E K D K AAGTTTGGCTTTTGGGGACCCAATTGCACAGAGAGAGGCTCCTGGTCAGGAGAAACATTTTCGATCTGTCCGCCCCTGAGAAAGACAAA Gene : Tyros Segment# : 9 : 121 1st Codon: 1 V R R N I F D L S A P E K D K F F A Y L T L A K H T I S S D GTGAGAAGGAATATCTTTGACCTCAGCGCTCCCGAAAAGGATAAGTTTTTCGCTTACCTCACCCTCGCCAAACACACAATCTCCAGCGAT : Tyros Gene Segment# : 10 Offset : 136 1st Codon : 1 F F A Y L T L A K H T I S S D Y V I P I G T Y G Q M K N G S TTCTTTGCCTATCTGGCACACTGGCTAAGCATACCATTAGCTCCGACTATGTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCC : Tyros Gene Segment# : 11 : 151 Offset 1st Codon : 1 YVIPIGTYGQMKNGSTPMFNDINIYDLFVW TACGTCATCCCTATCGGAACCTATGGCCAAATGAAAAACGGAAGCACCCCATGTTCAATGACATTAACATTTACGATCTGTTTGTGTGG : Tyros Gene Segment# : 12 Offset : 166 1st Codon : 1

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```
T P M F N D I N I Y D L F V W M H Y Y V S M D A L L G G S E
 ACCCCTATGTTTAACGATATCAATATCTATGACCTCTTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGAA
         : Tyros
 Segment# : 13
Offset
        : 181
1st Codon: 1
M H Y Y V S M D A L L G G S E I W R D I D F A H E A P A F L
: Tyros
Segment# : 14
Offset
        : 196
1st Codon : 1
 I W R D I D F A H E A P A F L P W H R L F L L R W E Q E I Q
ATCTGGAGGGATATCGATTTCGCTCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGAAATCCAA
         : Tyros
Gene
Segment# : 15
Offset
        : 211
1st Codon : 1
    P W H R L F L L R W E Q E I Q K L T G D E N F T I P Y W D W
CCCTGGCACAGACTGTTTCTGCTCAGGTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAATCCCTTACTGGGACTGG
Gene
         : Tyros
Segment# : 16
Offset
        : 226
1st Codon : 1
 K L T G D E N F T I P Y W D W R D A E K C D I C T D E Y M G
AAGCTCACCGGAGACGAAAACTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGA
        : Tyros
Gene
Segment# : 17
Offset
1st Codon : 1
 AGGGATGCCGAAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCCGCTAGCTTT
Gene
        : Tyros
Segment# : 18
Offset
        : 256
1st Codon: 1
G Q H P T N P N L L S P A S F F S S W Q I V C S R L E E Y N
GGCCAACACCCTACCAATCCCAATCTGCTCAGCCCTGCCTCCTTCTTTAGCTCCTGGCAAATCGTCTGCTCCAGGCTCGAGGAATACAAT
Gene
        : Tyros
Segment# : 19
        : 271
Offset
1st Codon : 1
F S S W Q I V C S R L E E Y N S H Q S L C N G T P E G P L R
TTCTCCAGCTGGCAGATTGTGTGTAGCAGACTGGAAGAGTATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGA
        : Tyros
Segment# : 20
        : 286
1st Codon : 1
S H Q S L C N G T P E G P L R R N P G N H D K S R T P R L P
AGCCATCAGTCCCTGTGTAACGGAACCCCTGAGGGACCCCTCAGGAGAAACCCTGGCAATCACGATAAGTCCAGGACACCCAGACTGCCT
Segment# : 21
Offset
        : 301
1st Codon : 1
R N P G N H D K S R T P R L P S S A D V E F C L S L T Q Y E
AGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCGCTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAA
Gene
        : Tyros
Segment# : 22
Offset : 316
1st Codon : 1
S S A D V E F C L S L T Q Y E S G S M D K A A N F S F R N T AGCTCCGCCGATGTGGATTCTGTCTCTCCTGACACACTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACA
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Gene : Tyros Segment# : 23 Offset S G S M D K A A N F S F R N T L E G F A S P L T G I A D A S Gene : Tyros Segment# : 24 Offset : 346 1st Codon : 1 LEGFASPLTGIADASQSSMHNALHIYMNGT CTGGAAGGCTTTGCCTCCCCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCATGCATAACGCTCTGCATATCTATATGAATGGCACA Segment# : 25 : 361 1st Codon : 1 Q S S M H N A L H I Y M N G T M S Q V Q G S A N D P I F L L CAGTCCAGCATGCACAATGCCCTCCACATTTACATGAACGGAACCATGAGCCAAGGCTCCGCCAATGACCCTATCTTTCTGCTC : Tyros Segment# : 26 Offset : 376 1st Codon: 1
MSQVQGSANDPIFLLHHAFVDSIFEQWLQR ATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCGTCGACCTCCATCTTTGAGCAATGGCTCCAGAGA Gene : Tyros : 27 Segment# : 391 Offset 1st Codon : 1 H H A F V D S I F E Q W L Q R H R P L Q E V Y P E A N A P I CACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCATAGGCCTCTGCAAGAGGGTCTACCCTGAGGCTAACGCTCCCATT : Tyros Segment# : 28 Offset : 406 H R P L Q E V Y P E A N A P I G H N R E S Y M V P F I P L Y CACAGACCCCTCCAGGAAGTGTATCCCGAAGCCAATGCCCCTATCGGACACAATAGGGAAAGCTATATGGTCCCCTTTATCCCTCTGTAT : Tyros Gene Segment# : 29 : 421 Offset 1st Codon : 1 G H N R E S Y M V P F I P L Y R N G D F F I S S K D L G Y D GGCCATAACAGAGAGTCCTACATGGTGCCTTTCATTCCCCTCTACAGAAACGGAGACTTTTTCATTAGCTCCAAGGATCTGGGATACGAT Gene : Tyros Segment# : 30 : 436 RNGDFFISSKDLGYDYSYLQDSDPDSFQDY AGGAATGGCGATTTCTTTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACTCCTTCCAAGACTAT : Tyros Segment# : 31 Offset : 451 1st Codon : 1 Y S Y L Q D S D P D S F Q D Y I K S Y L E Q A S R I W S W L TACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTC : Tyros Gene Segment# : 32 Offset : 466 1st Codon : 1 I K S Y L E Q A S R I W S W L L G A A M V G A V L T A L L A 

Figure 27 (Cont)

: Tyros

Gene

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```
Segment# : 33
1st Codon : 1
L G A A M V G A V L T A L L A G L V S L L C R H K R K Q L P CTGGGAGCCGCTATGGTCGCCGCTCTGCTCGCCCGGACTGGTCAGCCTCTGTGTAGGCATAAGAGAAAGCAACTGCCT
         : Tyros
Segment# : 34
        : 496
Offset
1st Codon : 1
 G L V S L L C R H K R K ,Q L P E E K Q P L L M E K E D Y H S
GGCCTCGTGCTCTGCTGCAGACACAAAAGGAAACAGCTCCCCGAAGAGAAACAGCCTCTGCTCATGGAAAAAGGAAGACTATCACTCC
         : Tyros
Segment# : 35
Offset
        : 511
1st Codon : 1
 E E K Q P L L M E K E D Y H S L Y Q S H L A A
GAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCC
        : TRP2
Gene
Segment# : 1
Offset
 A A M S P L W W G F L L S C L G C K I L P G A Q G Q F P R V
GCCGCTATGTCCCCCCTCTGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCCGGAGCCCAAGGCCAATTCCCTAGGGTC
        : TRP2
Gene
Segment# : 2
Offset
        : 16
1st Codon: 1
G C K I L P G A Q G Q F P R V C M T V D S L V N K E C C P R
GGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAGCCTCGTGAATAAGGAATGCTGTCCCAGA
Gene
Segment# : 3
1st Codon: 1
CMTVDSLVNKECCPRLGAESANVCGSQQGR
Gene
        : TRP2
Segment# : 4
        : 46
Offset
1st Codon : 1
L G A E S A N V C G S Q Q G R G Q C T E V R A D T R P W S G
CTGGGAGCCGAAAGCGCTAACGTCTGCGGAAGCCAACAGGGAAGGGGACAGTGTACCGAAGTGAGAGCCGATACCAGACCCTGGAGCGGA
        : TRP2
Gene
Segment# : 5
Offset
        : 61
1st Codon : 1
G Q C T E V R A D T R P W S G P Y I L R N Q D D R E L W P R
GGCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGA
Gene
       : 6
Segment#
PYILRNQDDRELWPRKFFHRTCKCTGNFAGCCCTATATCCTCAGGAATCAGGAACCTTGCCGGAAACTTTGCCGGA
        : TRP2
Segment# : 7
Offset
        : 91
K F F H R T C K C T G N F A G Y N C G D C K F G W T G P N C
AAGTTTTTCCATAGGACATGCAAATGCACAGGCAATTTCGCTGGCTATAACTGTGGCGATTGCAAATTCGGATGGACAGGCCCTAACTGT
        : TRP2
Segment# : 8
Offset
        : 106
```

Figure 27 (Cont)

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YNCGDCKFGWTGPNCERKKPPVIRQNIHSL Segment# : 9 Offset : 121 1st Codon : 1 ERKKPPVIRQNIHSLSPQEREQFLGALDLA Segment# : 10 Offset : 136 1st Codon : 1 S P Q E R E Q F L G A L D L A K R V H P D Y V I T T Q H W AGCCCTCAGGAAAGGGAACAGTTTCTGGGAGCCCTCGACCTCGCCAAAAAGAGAGTGCATCCCGATTACGTCATCACAACCCCAACACTGG : TRP2 Gene Segment# : 11 Offset : 151 1st Codon : 1 K K R V H P D Y V I T T Q H W L G L L G P N G T Q P Q F A N AAGAAAAGGGTCCACCCTGACTATGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACACAGCCTCAGTTTGCCAAT : TRP2 Gene Segment# : 12 Offset 1st Codon : 1 L G L L G P N G T Q P Q F A N C S V Y D F F V W L H Y Y S V  $\tt CTGGGACTGGTCGGCCCTAACGGAACCCCAACCCCAATTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTC$ : TRP2 Segment# : 13 Offset : 181 TGCTCCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACACTGCTCGGCCCTGGCAGACCCTATAGGGCTATCGAT : TRP2 Gene Segment# : 14 : 196 Offset 1st Codon : 1 R D T L L G P G R P Y R A I D F S H Q G P A F V T W H R Y H AGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCCGCTTTCCTCACCTGGCACAGATACCAT : TRP2 Segment# : 15 Offset : 211 F S H Q G P A F V T W H R Y H L L C L E R D L Q R L I G N E TTCTCCCACCAAGGCCCTGCCTTTGTGACATGGCATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGAA Gene · TRP2 Segment# : 16 Offset : 226 1st Codon: 1 L L C L E R D L Q R L I G N E S F A L P Y W N F A T G R N E CTGCTCTGCCTCGAGAGAGCCTCCAGAGACTGATTGGCAATGAGTCCTTCGCTCTGCCTTACTGGAACTTTGCCACAGGCAGAAACGAA : TRP2 Gene Segment# : 17 Offset : 241 S F A L P Y W N F A T G R N E C D V C T D Q L F G A A R P D : TRP2 Segment# : 18 : 256 1st Codon : 1 A R P D D P T L I S R N S R F S S W E CDVCTDQLFGA

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TGCGATGTGTGTACCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAA : TRP2 Segment# : 19 Offset : 271 1st Codon : 1 D P T L I S R N S R F S S W E T V C D S L D D Y N H L V T L : TRP2 Segment# : 20 Offset : 286 1st Codon : 1 T V C D S L D D Y N H L V T L C N G T Y E G L L R R N Q M G ACCGTCTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAACCAAATGGGA : TRP2 Segment# : 21 Offset : 301 1st Codon : 1 C N G T Y E G L L R R N Q M G R N S M K L P T L K D I R D C TGCAATGCCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGGCAGAAACTCCATGAAACTGCCTACCCTCAAGGATATCAGAGACTGT : TRP2 Gene Segment# : 22 Offset : 316 1st Codon : 1 R N S M K L P T L K D I R D C L S L Q K F D N P P F F Q N S Gene Segment# : 23 Offset : 331 LSLQKFDNPPFFQNSTFSFRNALEGFDKAD CTGTCCCTGCAAAAGTTTGACAATCCCCCTTTCTTTCAGAATAGCACATTCTCCTTCAGAAACGCTCTGGAAGGCTTTGACAAAGCCGAT Gene : TRP2 Segment# : 24 Offset : 346 1st Codon : 1 T F S F R N A L E G F D K A D G T L D S O V M S L H N L V H ACCTTTAGCTTTAGGAATGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCAT : TRP2 Segment# : 25 Offset : 361 1st Codon : 1 G T L D S Q V M S L H N L V H S F L N G T N A L P H S A A Gene : TRP2 Segment# : 26 : 376 1st Codon : 1 S F L N G T N A L P H S A A N D P I F V V L H S F T D A I F  ${\tt AGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCCGCCGCTAACGATCCCATTTTCGTCGTGCTCCACTCCTTCACAGACGCTATCTTT}$ : TRP2 Gene Segment# : 27 Offset : 391 D P I F V V L H S F T D A I F D E W M K R F N P P A D A W P GACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGATGAGTGGATGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCT Gene : TRP2 Segment# : 28 Offset : 406 

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: TRP2 Segment# : 29 Offset : 421 1st Codon : 1 Q E L A P I G H N R M Y N M V P F F P P V T N E E L F L T S : TRP2 Segment# : 30 : 436 Offset 1st Codon : 1 P F F P P V T N E E L F L T S D Q L G Y S Y A I D L P V S V  $\tt CCCTTTTTCCCTCCCGTCACCAATGAGGAACTGTTTCTGACAAGCGATCAGCTCGGCTATAGCTATGCCATTGACCTCCCCGTCAGCGTC$ : TRP2 Gene Segment# : 31 Offset : 451 DQLGYSYAIDLPVSVEETPGWPTTLLVVMG GACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACACTGCTCGTGGTCATGGGA Gene : TRP2 Segment# : 32 Offset : 466 1st Codon : 1 EETPGWPTTLLVVMGTLVALVGLFVLLAFL Gene Segment# : 33 : 481 : TRP2 Gene Segment# : 34 Offset : 496 1st Codon : 1 Q Y R R L R K G Y T P L M E T H L S S K R Y T E E A A A CAGTATAGGAGACTGAGAAAGGGATACACCCCTCATGGAAACCCATCTGTCCAGCAAAAGGTATACCGAAGAGGCTGCCGCT Segment# : 1 Offset 1st Codon : 1 A A M A V Q G S Q R R L L G S L N S T P T A I P Q L G L A A GCCGCTATGGCTGTGCAAGGCTCCCAGAGAAGGCTCCTGGGAAGCCTCAACTCCACCCCTACCGCTATCCCTCAGCTCGGCCTCGCCGCT Segment# : 2 Offset : 16 1st Codon: 1 LNSTPTAIPQLGLAANQTGARCLEVSISDG CTGAATAGCACACCCACAGCCATTCCCCAACTGGGACTGGCTGCCAATCAGACAGGCGCTAGGTGTCTGGAAGTGTCCATCTCCGACGGA Gene : MC1R Segment# : 3 Offset : 31 1st Codon : 1 N Q T G A R C L E V S I S D G L F L S L G L V S L V E N A L AACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAGCGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGTCGAGAATGCCCTC : MC1R Gene Segment# : 4 1st Codon : 1 L F L S L G L V S L V E N A L V V A T I A K N R N L H S P M CTGTTTCTGTCCCTGGGACTGGTCAGCCTCGTGGAAAACGCTCTGGTCGTGGCTACCATTGCCAAAAACAGAAACCTCCACTCCCCCATG : MC1R Segment# : 5

Figure 27 (Cont)

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```
Offset
1st Codon: 1
V V A T I A K N R N L H S P M Y C F I C C L A L S D L L V S
GTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCTATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTGTCC
        : MC1R
Gene
Segment# : 6
        : 76
Offset
1st Codon : 1
 Y C F I C C L A L S D L L V S G T N V L E T A V I L L E A
TACTGTTTCATTTGCTGTCTGGCTCTGTCCGACCTCCTGGTCAGCGGAACCAATGTGCTCGAGACAGCCGTCATCCTCCTGCTCGAGGCT
        : MC1R
Gene
Segment# : 7
Offset
1st Codon : 1
 G T N V L E T A V I L L E A G A L V A R A A V L Q Q L D N
GGCACAAACGTCCTGGAAACCGCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGTGGCTAGGGCTGCCGTCCTGCAACAGCTCGACAAT
        : MC1R
Gene
Segment# : 8
Offset
        : 106
1st Codon: 1
GALVARAAVLQQLDNVIDVITCSSMLSSLC
GGCGCTCTGGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCATCGATGTGATTACCTGTAGCTCCATGCTCAGCTCCCTGTGT
        : MC1R
Segment# : 9
        : 121
1st Codon : 1
V I D V I T C S S M L S S L C F L G A I A V D R Y I S I F Y GTGATTGACGTCACATGCTCCAGCATGCTGTCCAGCCTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTCTAT
        : MC1R
Segment# : 10
Offset
        : 136
1st Codon: 1
F L G A I A V D R Y I S I F Y A L R Y H S I V T L P R A P R
TTCCTCGGCGCTATCGCTGTGGATAGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGA
        : MC1R
Gene
Segment# : 11
       : 151
Offset
1st Codon : 1
ALRYHSIVTLPRAPRAVAAIWVASVVFSTL
GCCCTCAGGTATCACTCCATCGTCACCCTCCCCAGAGCCCCTAGGGCTGTGGCTGCCATTTGGGTCGCCTCCGTGGTCTTCTCCACCCTC
        : MC1R
Segment# : 12
       : 166
A V A A I W V A S V V F S T L F I A Y Y D H V A V L L C L V
Gene
        : MC1R
Segment# : 13
Offset
       : 181
1st Codon: 1
FIAYYD H V A V L L C L V V F F L A M L V L M A V L Y V
Gene
        : MC1R
Segment# : 14
       : 196
Offset
1st Codon: 1
V F F L A M L V L M A V L Y V H M L A R A C Q H A Q G I A R
GTGTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCATATGCTCGCCAGAGCCTGTCAGCATGCCCAAGGCATTGCCAGA
        : MC1R
Segment# : 15
       : 211
Offset
1st Codon : 1
```

Figure 27 (Cont)

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H M L A R A C Q H A Q G I A R L H K R Q R P V H Q G F G L K CACATGCTGGCTAGGGCTTGCCAACACGCTCAGGGAATCGCTCCACAAAAGGCCAAGGCCTGTGCATCAGGGATTCGGACTGAAA Segment# : 16 Offset : 226 L H K R Q R P V H Q G F G L K G A V T L T I L L G I F F L C CTGCATAAGAGACAGAGACCCGTCCACCAAGGCTTTGGCCTCAAGGGAGCCGTCACCCTCACCATTCTGCTCGGCATTTTCTTTTCTGTGT Segment# : 17 : 241 Offset 1st Codon : 1 G A V T L T I L L G I F F L C W G P F F L H L T L I V L C P : MC1R Segment# : 18 : 256 Offset 1st Codon: 1 W G P F F L H L T L I V L C P E H P T C G C I F K N F N L F TGGGACCCTTTTTCCTCCACCTCATCGTCCTCTTGTCCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTT : MC1R Gene Segment# : 19 Offset : 271 1st Codon: 1
E H P T C G C I F K N F N L F L A L I I C N A I I D P L I Y GAGCATCCCACATGCGGATGCATTTTCAAAAACTTTAACCTCTTCCTCGCCCTCATCATTTGCAATGCCATTATCGATCCCCTCATCTAT : MC1R Segment# : 20 : 286 1st Codon : 1 LALIICNAIIDPLIYAFHSQELRRTLKEVL CTGGCTCTGATTATCTGTAACGCTATCATTGACCCTCTGATTTACGCTTTCCATAGCCAAGAGCTCAGGAGAACCCTCAAGGAAGTGCTC : MC1R Gene Segment# : 21 Offset : 301 GCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCC : MUC1F Gene Segment# Offset 1st Codon : 1 A A M T P G T Q S P F L L L L T V L T V V T G S G H A S GCCGCTATGACACCCGGAACCCAAAGCCCTTTCTTTCTGCTCCTGCTCCTGACAGTGCTCACCGTCGTGACAGGCTCCGGCCATGCCTCC : MUC1F Segment# : 2 LLTVLTVVTGSGHASSTPGGEKETSATQRS CTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGACACGCTAGCTCCACCCCTGGCGGAGAGAAAGAGACAAGCGCTACCCAAAGGTCC Gene : MUC1F Segment# : 3 Offset : 31 1st Codon: 1 S T P G G E K E T S A T Q R S S V P S S T E K N A V S M T S AGCACACCGGAGGCGAAAAGGAAACCTCCGCCACACAGAGAAGAGCTCCGTGCCTAGCTCCACCGAAAAGAATGCCGTCAGCATGACCTCC : MUC1F Gene Segment# : 4 Offset . : 46 1st Codon : 1 SVPSSTEKNAVSMTSSVLSSHSPGSGSSTT AGCGTCCCCTCCAGCACAGAGAAAAACGCTGTGTCCATGACAAGCTCCGTGCTCAGCTCCCACCCCGGGAAGCGGAAGCTCCACCACA

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```
Gene
        : MUC1F
Segment# : 5
Offset
       : 61
1st Codon: 1
S V L S S H S P G S G S S T T Q G Q D V T L A P A T E P A S
: MUC1F
Gene
Segment# : 6
       : 76
Offset
1st Codon: 1
O G Q D V T L A P A T E P A S G S A A T W G Q D V T S V P V
CAGGGACAGGATGTGACACTGGCTCCCGCTACCGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTC
Gene
       : MUC1F
Segment# : 7
Offset
       : 91
1st Codon: 1
G S A A T W G Q D V T S V P V T R P A L G S T T P P A H D V
GGCTCCGCCGCTACCTGGGGCCAAGACGTCACCTCCGTGCCTGTGACAAGGCCTGCCCTCGGCTCCACCACACCCCCTGCCCATGACGTC
       : MUC1F
Gene
Segment# : 8
       : 106
Offset
1st Codon: 1
TRPALGSTTPPAHDVTSAPDNKAA
ACCAGACCCGCTCTGGGAAGCACAACCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAAGCCGCT
       : MUC1R
Gene
Segment# : 1
1st Codon : 1
A A N R P A L G S T A P P V H N V T S A S G S A S G S A S T
GCCGCTAACAGACCCGCTCTGGGAAGCACAGCCCCTCCCGTCCACAATGTGACAAGCGCTAGCGGAAGCGCTAGCGGAAGCGCTAGCACAC
       : MUC1R
Segment# : 2
Offset
lst Codon: 1
N V T S A S G S A S G S A S T L V H N G T S A R A T T T P A
AACGTCACCTCCGCCTCCGGCTCCGCCTCCGCCTCCACCCTCGTGCATAACGGAACCTCCGCCAGAGCCACAACCACACCCGCT
       : MUC1R
Gene
Segment#
      : 3
       : 31
Offset
1st Codon : 1
LVHNGTSARATTTPASKSTPFSIPSHHSDT
CTGGTCCACAATGGCACAAGCGCTAGGGCTACCACAACCCCTGCCTCCAAGTCCACCCCTTTCTCCATCCCTAGCCATCACTCCGACACA
       : MUC1R
Gene
Segment# : 4
Offset : 46
S K S T P F S I P S H H S D T P T T L A S H S T K T D A S S
: MUC1R
Segment# : 5
Offset
       : 61
1st Codon : 1
p T T L A S H S T K T D A S S T H H S S V P P L T S S N H S
CCCACAACCCTCGCCTCCCACTCCACCAAAACCGATGCCTCCAGCACACACCATAGCTCCGTGCCTCCCCTCACCTCCAGCAATCACTCC
Gene
       : MUC1R
Segment# : 6
       : 76
Offset
1st Codon : 1
T H H S S V P P L T S S N H S T S P Q L S T G V S F F F L S
: MUC1R
Gene
```

Figure 27 (Cont)

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Segment# : 7 Offset 1st Codon: 1 T S P O L S T G V S F F F L S F H I S N L Q F N S S L E D P ACCTCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGCTTTCACATTGCAATCTGCAATTCAATAGCTCCCTGGAAGACCCT : MUC1R Gene Segment# : 8 Offset : 106 1st Codon : 1 PHISNLQFNSSLEDPSTDYY QELQRDISE M Segment# : 9 : 121 Offset 1st Codon: 1
S T D Y Y Q E L Q R D I S E M F L Q I Y K Q G G F L G L S N AGCACAGACTATTACCAAGAGCTCCAGAGAGACATTAGCGAAATGTTTCTGCAAATCTATAAGCAAGGCGGATTCCTCGGCCTCAGCAAT Gene Segment# : 10 Offset 1st Codon: 1
FLQIYKQGGFLGLSNIKFRPGSVVVQLTLA TTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGACTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGTACAACTGACACTGGCT : MUC1R Segment# : 11 Offset : 151 1st Codon : 1 I K P R P G S V V Q L T L A F R E G T I N V H D V E T Q F : MUC1R Segment# : 12 -: 166 Offset 1st Codon: 1 FREGTINVHDVETQFNQYKTEAASRYNLT TTCAGAGAGGGAACCATTAACGTCCACGATGTGGAAACCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACCTCACCATT : MUC1R Segment# : 13 NQYKTEAASRYNLTISDVSVSDVPFPFSAQ AACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCTTTCTCCGCCCAA : MUC1R Gene Segment# : 14 : 196 Offset 1st Codon : 1 S D V S V S D V P F P F S A Q S G A G V P G W G I A L L V L AGCGATGTGTCCGTGTCCGACGTCCCCTTTCCCTTTAGCGCTCAGTCCGGCGCTCGCGGCGTCCCCGGATGGGGAATCGCTCTGCTGCTGCTC : MUC1R Gene Segment# : 15 Offset 1st Codon: 1 S G A G V P G W G I A L L V L V C V L V A L A I V Y L I A L AGCGGAGCCGGAGTGCCTGGGGGCATTGCCCTCCTGGTCCTGGTCTGCGTCCTGGTCGGCCCTCGCCATTGTGTATCTGATTGCCCTC: MUC1R Gene Segment# : 16 : 226 Offset 1st Codon: 1 V C V L V A L A I V Y L I A L A V C Q C R R K N Y G Q L D I : MUC1R Segment# : 17 : 241

169/216 1st Codon: 1 A V C Q C R R K N Y G Q L D I F P A R D T Y H P M S E Y P T GCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACA Gene : MUC1R Segment# : 18 Offset : 256 1st Codon : 1 F P A R D T Y H P M S E Y P T Y H T H G R Y V P P S S T D R Gene : MUC1R Segment# : 19 Offset : 271 1st Codon : 1 Y H T H G R Y V P P S S T D R S P Y E K V S A G N G G S S L Gene : MUC1R Segment# : 20 Offset : 286 1st Codon: 1
SPYEKVSAGNGGSSLSYTNPAVAASANLA AGCCCTTACGAAAAGGTCAGCGCTGGCAATGGCGGAAGCTCCCTGTCCTACACAAACCCTGCCGTCGCCGCTGCCTCCCCAATCTGGCT Gene : MUC1R Segment# : 21 Offset 1st Codon : 1 S Y T N P A V A A A S A N L A A AGCTATACCAATCCCGCTGTGGCTGCCGCTAGCGCTAACCTCGCCGCT Segments in scrambled order: TRP2 #6
PYILRNQDDRELWPRKFFHRTCKCTAACCCCAAACCTTTTCCCCCCA CCCTATATCCTCAGGAATCAGGATGACAGAGGCTCTGGCCTAGGAAATTCTTTCACAGAACCTGTAAGTGTACCGGAAACTTTGCCGGA Tyros #30
RNGDFFISSKDLGYDYSYLQDSDPDSFQDY AGGAATGCCGATTTCTTTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACTCCTTCCAAGACTAT A A P A F L T W H R Y H L L R L E K D M Q E M L Q E P S F S  ${\tt GCCGCTCCCGCTTTCCTCACCTGGCACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTTCTTCCC}$ Ğ H N R E S Y M V P F I P L Y R N G D F F I S S K D L G Y D  ${\tt GGCCATAACAGAGAGTCCTACATGGTGCCTTTCATTCCCCTCTACAGAAACGGAGACTTTTTCATTAGCTCCAAGGATCTGGGATACGAT}$ L L C L E R D L Q R L I G N E S F A L P Y W N F A T G R N E CTGCTCTGCCTCGAGAGAGCCTCCAGAGACTGATTGGCAATGAGTCCTTCGCTCTGCCTTACTGGAACTTTGCCACAGGCAGAAACGAA gp100 #23
T T E V V G T T P G Q A P T A E P S G T T S V Q V P T T E V ACCACAGAGGTCGTGGGAACCACCCGGACAGCCTCCGGCACACCTCCGTGCAAGTGCCTACCACAGAGGTC S T D Y Y Q E L Q R D I S E M F L Q I Y K Q G G F L G L S N AGCACAGACTATTACCAAGAGCTCCAGAGAGACATTAGCGAAATGTTTCTGCAAATCTATAAGCAAGGCGGATTCCTCGGCCTCAGCAAT gp100 #36 ACMEISSPGCQPPAQRLCQPVLPSPACQLV

Figure 27 (Cont)

GCCTGTATGGAAATCTCCAGCCTGGCTGTCAGCCTCCCGCTCAGAGACTGTGTCAGCCTGTGCCCTCCCCCGCTTGCCAACTGGTC

D Q L G Y S Y A I D L P V S V E E T P G W P T T L L V V M G

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GACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACACTGCTCGTGGTCATGGGA

TRP-1 #7

T E D G P I R R N P A G N V A R P M V Q R L P E P Q D V A Q ACCGAAGACGCACCCATTAGGAGAAACCCTGCCGGAAACGTCGCCAGACCCATGGTGCAAAGGCTCCCCGAACCCCAAGACGTCGCCCAA

C M T V D S L V N K E C C P R L G A E S A N V C G S Q Q G R 

MUCIR #13

N Q Y K T E A A S R Y N L T I S D V S V S D V P F P F S A Q AACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCTTTCTCCGCCCAA

A A M S P L W W G F L L S C L G C K I L P G A Q G Q F P R V GCCGCTATGTCCCCCCTCTGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCCGGAGCCCAAGGCCAATTCCCTAGGGTC

A D L S Y T W D F G D S S G T L I S R A L V V T H T Y L E P 

gp100 #27 L A E M S T P E A T G M T P A E V S I V V L S G T T A A Q V CTGGCTGAGATGAGCACACCCGAAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTC

G S A A T W G Q D V T S V P V T R P A L G S T T P P A H D V 

L H K R Q T P V H Q G F G L K G A V T L T I L L G I F F L C 

 $\begin{smallmatrix} L&A&L&I&I&C&N&A&I&I&D&P&L&I&Y&A&F&H&S&Q&E&L&R&R&T&L\cdot K&E&V&L\\ \end{smallmatrix}$ CTGGCTCTGATTATCTGTAACGCTATCATTGACCCTCTGATTTACGCTTTCCATAGCCAAGAGCTCAGGAAACCCTCAAGGAAGTGCTC

K F F H R T C K C T G N F A G Y N C G D C K F G W T G P N C AAGTTTTTCCATAGGACATGCAAATGCACAGGCAATTTCGCTGGCTATAACTGTGGCGATTGCAAATTCGGATGGACAGGCCCTAACTGT

LSLOKFDNPPFFQNSTFSFRNALEGFDKAD CTGTCCCTGCAAAAGTTTGACAATCCCCCTTTCTTTCAGAATAGCACATTCTCCTTCAGAAACGCTCTGGAAGGCTTTGACAAAGCCGAT

 $\begin{smallmatrix} S&K&S&T&P&F&S&I&P&S&H&H&S&D&T&P&T&T&L&A&S&H&S&T&K&T&D&A&S&S\\ \end{smallmatrix}$ 

A A N R P A L G S T A P P V H N V T S A S G S A S G S A S T 

C N G T Y E G L L R R N Q M G R N S M K L P T L K D I R D C  ${\tt TGCAATGGCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGGCAGAAACTCCATGAAACTGCCTACCCTCAAGGATATCAGAGACTGT}$ 

H H S S V P P L T S S N H S T S P Q L S T G V S F F F L S 

FIAYYDHVAVLLCLVVFFLAMLVLMAVLYV 

Tyros #16

K L T G D E N F T I P Y W D W R D A E K C D I C T D E Y M G

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AAGCTCACCGGAGACGAAAACTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGA gp100 #32 . LRLVKRQVPLDCVLYRYGSFSVTLDIVQGI CTGAGACTGGTCAAGAGACAGGTCCCCCTCGACTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATT MUC1R #10 FLQIYKQGGFLGLSNIKFRPGSVVVQLTLA TTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGACTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCCAACTGACACTGGCT MC1R #9 V I D V I T C S S M L S S L C F L G A I A V D R Y I S I F Y GTGATTGACGTCATCACATGCTCCAGCATGCTGTCCAGCCTCTGCTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTCTAT R N P G N H D K S R T P R L P S S A D V E F C L S L T Q Y E AGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCGCTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAA F D E W L R R Y N A D I S T F P L E N A P I G H N R Q Y N M V S L A D T N S L A V V S T Q L I M P G Q E A G L G Q V P L GTGTCCTGGCTGACACAAACTCCCTGGCTGTGGTCAGCACACAGCTCATCATGCCCGGACAGGAAGCCGGACTGGGACAGGTCCCCCTC gp100 #20
G P V T A Q V V L Q A A I P L T S C G S S P V P G T T D G H  ${\tt GGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTGTGCCTGGCACAACCGATGGCCAT}$ K F G F W G P N C T E R R L L V R R N I F D L S A P E K D K AAGTTTGGCTTTTGGGGACCCAATTGCACAGAGAGAGGCTCCTGGTCAGGAGAACATTTTCGATCTGTCCGCCCCTGAGAAAGACAA L G T H T M E V T V Y H R R G S R S Y V P L A H S S S A F T CTGGGAACCCATACCATGGAGGTCACCGTCTACCATAGGAGAGGGCTCCAGGTCCTACGTCCCCTCGCCCATAGCTCCAGCGCTTTCACA A V A A I W V A S V V F S T L F I A Y Y D H V A V L L C L V GCCGTCGCCGCTATCTGGGTGGCTAGCGTCGTGTTTAGCACACTGTTTATCGCTTACTATGACCATGTGGCTGTGCTCCTGTGTCTGGTC G T L D S Q V M S L H N L V H S F L N G T N A L P H S A A N G C W Y C R R N G Y R A L M D K S L H V G T Q C A L T R R GGCTGTTGGTATTGCAGAAGGAGAAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGA Tyros #15
PWHRLFLLRWEQEIQKLTGDENFTIPYWDW CCCTGGCACAGACTGTTTCTGCTCAGGTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAATCCCTTACTGGGACTGG A A M A V Q G S Q R R L L G S L N S T P T A I P Q L G L A A V V A T I A K N R N L H S P M Y C F I C C L A L S D L L V S GTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCTATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTGTCC Q S S M H N A L H I Y M N G T M S Q V Q G S A N D P I F L L CAGTCCAGCATGCACAATGCCCTCCACATTTACATGAACGGAACCATGAGCCAAGTGCAAGGCTCCGCCAATGACCCTATCTTTCTGCTC Ğ Q H P T N P N L L S P A S F F S S W Q I V C S R L E E Y N GGCCAACACCCTACCAATCTGCTCAGCCTGCCTCCTTCTTTAGCTCCTGGCAAATCGTCTGCTCCAGGCTCGAGGAATACAAT

Figure 27 (Cont)

Y C[°]FICCLALS DLL V S G T N V L E T A V I L L E A

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D P T L I S R N S R F S S W E T V C D S L D D Y N H L V T L GACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGTGACTCCCTGGATGACTATAACCATCTGGTCACCCTC

TRPALGSTTPPAHDVTSAPDNKAA ACCAGACCCGCTCTGGGAAGCACAACCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAGCCGCT

Tyros #17

R D A E K C D I C T D E Y M G G Q H P T N P N L L S P A S F AGGGATGCCGAAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCCGCTAGCTTT

T F A L Q L H D P S G Y L A E A D L S Y T W D F G D S S G T ACCTTTGCCCTCCAGCTCCACGATCCCTCCGGCTATCTGGCTGAGGCTGACCTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACA

S S A D V E F C L S L T Q Y E S G S M D K A A N F S F R N T AGCTCCGCCGATGTGGAATTCTGTCTCTTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACA

G P T L I G A N A S F S I A L N F P G S Q K V L P D G O V I GGCCCTACCCTCATCGGAGCCAATGCCTCCTTCTCCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATT

W G P F F L H L T L I V L C P E H P T C G C I F K N F N L F TGGGGACCCTTTTTCCTCCACCTCACCCTCATCGTCCTGTGTCCCGAACACCCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTT

Q C S G N F M G F N C G N C K F G F W G P N C T E R R L L TGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATTCGGATTCTGGGGCCCTAACTGTACCGAAAGGACACTGCTC

Q Y R R L B K G Y T P L M E T H L S S K R Y T E E A A CAGTATAGGAGACTGAGAAAGGGATACACACCCCTCATGGAAACCCATCTGTCCAGCAAAAGGTATACCGAAGAGGCTGCCGCT

PLENAPIGHNRQYNMVPFWPPVTNTEMFVT CCCCTCGAGAATGCCCCTATCGGACACAATAGGCAATACAATATGGTCCCCTTTTGGCCTCCCGTCACCAATACCGAAATGTTTGTGACA

N F P G S Q K V L P D G Q V I W V N N T I I N G S Q V W G G AACTTTCCCGGAAGCCAAAAGGTCCTGCCTGACGGACAGGTCATCTGGGTGAATAACACAATCATTAACGGAAGCCAAGTGTGGGGCGGA

R P T A E A P N T T A G Q V P T T E V V G T T P G Q A P T A AGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACAACCCCTGGCCAAGCCCCTTACCGCT

S T P G G E K E T S A T Q R S S V P S S T E K N A V S M T S AGCACACCGGAAGGCGAAAAGGAAACCTCCGCCACACAGAGAAAGCTCCGTGCCTAGCTCCGCCGAAAAGAATGCCGTCAGCATGACCTCC

gp100 #42 LIYRRRLMKQDFSVPQLPHSSSHWLRLPRI CTGATTTACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCAGCTCCAGCTCCCACTGGCTGAGACTGCCTAGGATT

L G L L G P N G T Q P Q F A N C S V Y D F F V W L H Y Y S V CTGGGACTGCTCGGCCCTAACGGAACCCCAACTCGCTAACTGTAGCGTCTACGATTTCTTTTGTGTGGCTGCATTACTATAGCGTC

C L E V G L F D T P P F Y S N S T N S F R N T V E G Y S D P
TGCCTCGAGGTCGCCTCTTCGATACCCCTCCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCT

A A M D L V L K R C L L H L A V I G A L L A V G A T K V P R GCCGCTATGGATCTGGTCTGAAAAGGTGTCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGA

N Q T G A R C L E V S I S D G L F L S L G L V S L V E N A L

PCT/AU01/00622

### WO 01/090197

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 ${\tt AACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAGCGATGGCCTCTTCCTCAGCCTCGGCCTCGTCGAGGAATGCCCTC}. \\$ 

Tyros #23
S G S M D K A A N F S F R N T L E G F A S P L T G I A D A S AGCGGAAGCATGGACAAAGCCGCTAACTTTAGCTTTAGGATACCCTCGAGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCC

TYPOS #4

S P C G Q L S G R G S C Q N I L L S N A P L G P Q F P F T G

AGCCCTTGCGGACAGCTCAGCGGAAGGGGAAGCTGTCAGAATATCCTCCTGTCCAACGCTCCCCTCGGCCCTCAGTTTCCCTTTACCGGA

Tyros #13 , where the sum of the

TYYOS #35

E E K Q P L L M E K E D Y H S L Y Q S H L A A
GAGGAAAAGCAACCCCTCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCC

TRP2 #5

G Q C T E V R A D T R P W S G P Y I L R N Q D D R E L W P R

GGCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGA

MUC1F #4

S V P S S T E K N A V S M T S S V L S S H S P G S G S S T T

AGCGTCCCTCCAGCACAGAGAAAAACGCTGTGTCCATGACAAGCTCCGTGTCCAGCTCCCCCCGGAAGCGGAAGCTCCACCACA

Tyros  $\sharp 12$ T P M F N D I N I Y D L F V W M H Y Y V S M D A L L G G S E ACCCCTATGTTTAACGATATCAATATCTATGACCTCTCGGGGGAAGCGAA

gp100 #9 Q P V Y P Q E T D D A C I F P D G G P C P S G S W S Q K R S CAGCCTGTGTATCCCCAAGAGACAGACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCCGGCTCCTGGTCCCAGAAAAGGTCC

TRP-1 #6

D S L E D Y D T L G T L C N S T E D G P I R R N P A G N V A

GACTCCCTGGAAGACTATGACACACTGGGAACCCTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCT

gpl00 #8
W V N N T I I N G S Q V W G G Q P V Y P Q E T D D A C I F P
TGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGGAGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCT

gp100 #14 S R S Y V P L A H S S S A F T I T D Q V P F S V S V S Q L R AGCAGAAGCTATGGCCTCTGGCTCACTCCAGCTCCGCTTTACCGTTCAGGTCCCCTTTAGCGTCAGGTCCCCTTTAGCGTCAGCCTCAGCCCAACTGAGA

TRP-1 #16 V P F W P P V T N T E M F V T A P D N L G Y T Y E A A GTGCCTTTCTGGCCCCCTGTGACAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATGAGGCTGCC

TRP2 #13
C S V Y D F F V W L H Y Y S V R D T L L G P G R P Y R A I D
TGCTCCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACACTGCTCGGCCCTGGCAGACCCTATAGGGCTATCGAT

TYPOS #9

V R R N I F D L S A P E K D K F F A Y L T L A K H T I S S D

GTGAGAAGGAATATCTTTGACCTCAGCGCTCCCGAAAAGGATAAGTTTTTCGCTTACCTCACCCTCGCCAAACACAATCTCCAGCGAT

MART #2

K K G H G H S Y T T A E E A A G I G I L T V I L G V L L L I

AAGAAAGGCCATGGCCATAGCTATACCACAGCCGAAGAGGGCTGCCGGAATCGGAATCCTCACCGTCATCCTCGGCGTCCTGCTCCTGATT

gp100 #11 FVYVWK_.TWGQYWQVLGGPVSGLSIGTGRAM

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TTCGTCTACGTCTGGAAAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGGGAGAGCCATG

gp100 #12

. G G P V S G L S I G T G R A M L G T H T M E V T V Y H R R G 

I S T A P V Q M P T A E S T G M T P E K V P V S E V M G T T ATCTCCACCGCTCCGGATGCCCACAGCCGAAAGCACAGGCATGACCCCTGAGAAAGTGCCTGTGTCCGAGGTCATGGGAACCACA

Tyros #19
FSSWOIVCSRLEEYNSHOSLCNGTPEGPLR TTCTCCAGCTGGCAGATTGTGTAGCAGACTGGAAGAGTATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGA

D P I F V V L H S F T D A I F D E W M K R F N P P A D A W P  ${\tt GACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGATGAGTGGATGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCT}$ 

H M L A R A C Q H A Q G I A R L H K R Q R P V H Q G F G L K CACATGCTGGCTAGGGCTTGCCAACACGCTCAGGGAATCGCTAGGCTCCACAAAAGGCCAAAGGCCTGTGCATCAGGGATTCGGACTGAAA

L L T V L T V V T G S G H A S S T P G G E K E T S A T Q R S  $\tt CTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGCACACGCTAGCTCCACCCCTGGCGGAGAGAAAGAGACAAGCGCTACCCAAAGGTCC$ 

gp100 #44 F C S C P I G E N S P L L S G Q Q V A A TTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCT

TFSFRNALEGFDKADGTLDSQVMSLHNLVH ACCTTTAGCTTTAGGAATGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCAT

Tyros #20

S H Q S L C N G T P E G P L R R N P G N H D K S R T P R L P AGCCATCAGTCCCTGTGTAACGGAACCCCTGAGGGACCCCTCAGGAGAAACCCTGGCAATCACGATAAGTCCAGGACACCCAGACTGCCT

P F F P P V T N E E L F L T S D Q L G Y S Y A I D L P V S V CCCTTTTCCCTCCCGTCACCAATGAGGAACTGTTTCTGACAAGCGATCAGCTCGGCTATAGCTATGCCATTGACCTCCCCGTCAGCGTC

ERKKPPVIRQNIHSLSPQEREQFLGALDLA 

O E L A P I G H N R M Y N M V P F F P P V T N E E L F L T S 

gp100 #28 EVSIVVLSGTTAAQVTTTEWVETTARELPI 

T S P Q L S T G V S F F F L S F H I S N L Q F N S S L E D P ACCTCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGCTTTCACATTAGCAATCTGCAATTCAATAGCTCGCTGGAAGACCCT

MUCIR #19
YHTHGRYVPPSSTDRSPYEKVSAGNGGSSL TACCATACCCATGGCAGATACGTCCCCCCTAGCTCCACCGATAGGTCCCCCTATGAGAAAGTGTCCGCCGGAAACGGAGGCTCCAGCCTC

LFLSLGLVSLVENALVVATIAKNRNLHSPM CTGTTTCTGTCCCTGGGACTGGTCGTGGAAAACGCTCTGGTCGTGGCTACCATTGCCAAAAACAGAAACCTCCACTCCCCCATG

S F L N G T N A L P H S A A N D P I F V V L H S F T D A I F AGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCCGCCGCTAACGATCCCATTTTCGTCGTGCTCCACTCCTTCACAGACGCTATCTTT

A V C O C R R K N Y G Q L D I F P A R D T Y H P M S E Y P T

### 175/216

GCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACA

MC1R  $\sharp 14$  V F F L A M L V L M A V L Y V H M L A R A C Q H A Q G I A R GTGTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCATATGCTCGCCAGAGCCTGTCAGCATGCCCAAGGCATTGCCAGA

TRP-1 #10
S T N S F R N T V E G Y S D P T G K Y D P A V R S L H N L A
AGCACAAACTCCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCT

TRP-1 #3

L P Y W N F A T G K N V C D I C T D D L M G S R S N F D S T

CTGCCTTACTGGAACTTTGCCACAGGCAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACA

MUCIR #8'
F H I S N L Q F N S S L E D P S T D Y Y Q E L Q R D I S E M
TTCCATATCTCCAACCTCCAGCTTAACTCCAGCCTCGAGGATCCCTCCACCGATTACTATCAGGAACTGCAAAGGGATATCTCCGAGATG

S P Y E K V S A G N G G S S L S Y T N P A V A A A S A N L A AGCCCTTACGAAAAGGTCAGCGCTGGCAATGGCGGAAGCTCCCTGTCCTACACAAACCCTGCCGTCGCCGCTGCCTCCCGCCAATCTGGCT

Tyros #11 Y V I P I G T Y G Q M K N G S T P M F N D I N I Y D L F V W TACGTCATCCCTATCGGAACCTATGGCCAAATGAAAAACGGAAGCACCCATGTTCAATGACATTAACATTTACGATCTGTTGTGGG

gp100 #37
R L C Q P V L P S P A C Q L V L H Q I L K G G S G T Y C L N
AGGCTCTGCCAACCCGTCCTGCCTGCCTGCCTGCCTGCGCTCCGCACCCAAATCCTCAAGGGAGGCTCCGGCACATACTGTCTGAAT

gp100 #33 R Y G S F S V T L D I V Q G I E S A E I L Q  $\ddot{A}$  V P S G E G D AGGTATGGCTCCTTCTCCGTGACACTCGATATCGTCCAGGGAATCGAAAGCGCTGAGATTCTGCAAGCCGTCCCCTCCGGCGAAGGCGAT

Tyros #27
H H A F V D S I F E Q W L Q R H R P L Q E V Y P E A N A P I
CACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCCTAGGCCTCTGCAAGAGGTTACCCTGAAGGCTAACGCTCCCATT

TRP-1 #4 C T D D L M G S R S N F D S T L I S P N S V F S Q W R V V C TGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCAATAGCGTCTTCTCCCCAGTGGAGGGTCGTGTGT

MUCHR #21
S Y T N P A V A A A S A N L A A
AGCTATACCAATCCCGCTGTGGCTGCCGCTAGCGCTAACCTCGCCGCT

MC1R #19
E H P T C G C I F K N F N L F L A L I I C N A I I D P L I Y
GAGCATCCCACATGCGGATGCATTTTCAAAAACTTTAACCTCTTCCTCGCCCTCATCATTTGCAATGCCATTATCGATCCCCTCATCTAT

Tyros #26 M S Q V Q G S A N D P I F L L H H A F V D S I F E Q W L Q R ATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCGTCGACCTCCTTTTGAGCAATGGCTCCAGAGA

gp100 #19
L I S R A L V V T H T Y L E P G P V T A Q V V L Q A A I P L
CTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGTCAGGTCGTGCTCCCAGGCTGCCATTCCCCTC

TRP2 #17
S F A L P Y W N F A T G R N E C D V C T D Q L F G A A R P D

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WO 01/090197

### 176/216

gp100 #2

. VIGALLAVGATKVPRNQDWLGVSRQLRTKA GTGATTGGCGCTCTGCTCGCCGTCGGCGCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT

ALD G G N K H F L R N Q P L T F A L Q L H D P S G Y L A E GCCTCGACGGAGGCAATAAGCATTTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCTAGCGGATACCTCGCCGAA

C D V C T D Q L F G A A R P D D P T L I S R N S R F S S W E TGCGATGTGTGTACCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAA

**A A M P R E D A H F I Y G Y P K K G H G H S Y T T A E E A A** GCCCTATGCCTAGGGAAGACGCTCACTTTATCTATGGCTATCCCAAAAAGGGACACCGCACACTCCTACACAACCGCTGAGGAAGCCGCT

 $\texttt{T} \ \texttt{G} \ \texttt{K} \ \texttt{Y} \ \texttt{D} \ \texttt{P} \ \texttt{A} \ \texttt{V} \ \texttt{R} \ \texttt{S} \ \texttt{L} \ \texttt{H} \ \texttt{N} \ \texttt{L} \ \texttt{A} \ \texttt{H} \ \texttt{L} \ \texttt{F} \ \texttt{L} \ \texttt{N} \ \texttt{G} \ \texttt{T} \ \texttt{G} \ \texttt{G} \ \texttt{Q} \ \texttt{T} \ \texttt{H} \ \texttt{L} \ \texttt{S} \ \texttt{S}$ 

MUC1R #14
S D V S V S D V P F P F S A Q S G A G V P G W G I A L L V L AGCGATGTGTCCGTGTCCGACGTCCCCTTTCCCTTTAGCGCTCAGTCCGGCGCTGCGTCCCCGGATGGGGAATCGCTCTGCTCGTGCTC

S P Q E R E Q F L G A L D L A K K R V H P D Y V I T T Q H W AGCCCTCAGGAAAGGGAACAGTTTCTGGGAGCCCTCGACCTCGCCAAAAAGAGAGTGCATCACGATTACGTCATCACAACACCCAACACTGG

FAYLTLAKHTISSDYVIPIGTYGQMKNGS  ${\tt TTCTTTGCCTATCTGACACTGGCTAAGCATACCATTAGCTCCGACTATGTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCC}$ 

MUC1R #16 'V C V L V A L A I V Y L I A L A V C Q C R R K N Y G Q L D I 

C P Q E G F D H R D S K V S L Q E K N C E P V V P N A P P A TGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTCCCCAATGCCCCTCCCGCT

S V L S S H S P G S G S S T T Q G Q D V T L A P A T E P A S 

D E W M K R F N P P A D A W P Q E L A P I G H N R M Y N M V GACGAATGGATGAAGAGTTCAATCCCCCTGCCGATGCCTGGCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGGTC

A F H S Q E L R R T L K E V L T C S W A A GCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCC

F S H O G P A F V T W H R Y H L L C L E R D L Q R L I G N E TTCTCCCACCAAGGCCCTGCCTTTGTGACATGGCATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGAA

R P M V O R L P E P Q D V A Q C L E V G L F D T P P F Y S N AGGCCTATGGTCCAGAGACTGCCTGAGCCTCAGGATGTGGCTCAGTGTCTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAAT

TRP-1 #13 Q D P I F V L L H T F T D A V F D E W L R R Y N A D I S T F CAGGATCCCATTTTCGTCCTGCTCCACACATTCACAGACGCTGTGTTTTGACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTT

L G A E S A N V C G S Q Q G R G Q C T E V R A D T R P W S G

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TRP-1 #12

H L F L N G T G G Q T H L S S Q D P I F V L L H T F T D A V

CACCTCTTCCTCAACGGAACCGGAGCCCAACCCCATCTGTCCCAGCCAAGACCCTATCTTTGTGCTCCTGCATACCTTTACCGATGCCGTC

Tyros #34 . . G L V S L L C R H K R K Q L P E E K Q P L L M E K E D Y H S GGCCTCGTGTCCCTGCAGACACAAAGGAAACAGCTCCCCGAAGAGAACAGCCTCTGCTCATGGAAAAGGAAGACTATCACTCC

TRP2 #2

G C K I L P G A Q G Q F P R V C M T V D S L V N K E C Ć P R

GGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAGCCTCGTGAATAAGGAATGCTGTCCCAGA

gpl00 #43
Q L P H S S S H W L R L P R I F C S C P I G E N S P L L S G
CAGCTCCCCCATAGCTCCAGCCATTGGCTCAGGGCTCCCCAGAATCTTTTGCTCCTGCCCTATCGGAGAGAATAGCCCTCTGCTCAGCGGA

D G G P C P S G S W S Q K R S F V Y V W K T W G Q Y W Q V L
GACGGAGGCCCTTGCCCTAGCGGAAGCTGGGCCAAAAGAGAAGCTTTGTGTATGTGTAGGAAGACATGGGGACAGTATTGGCAAGTGCTC

Tyros #14

I W R D I D F A H E A P A F L P W H R L F L L R W E Q E I Q

ATCTGGAGGGATATCGATTCGCTCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGAAATCCAA

MUC1F #1
A A M T P G T Q S P F F L L L L T V L T V V T G S G H A S
GCCGCTATGACACCCGGAACCCAAAGCCCTTTCTTTCTGCTCCTGACAGTGCTCACCGTGACAGGCTCCCGGCCATGCCTCC

D K S L H V G T Q C A L T R R C P Q E G F D H R D S K V S L GACAAAAGCCTCCACGTCGGCACAAGTGTGCCCTCACCAGAAGGTGTCCCCCAAGAGGGATTCGATCACAGAGACTCCAAGGTCAGCCTC

MUCH #2

N V T S A S G S A S G S A S T L V H N G T S A R A T T T P A

AACGTCACCTCCGCCTCCGGCTCCGCCTCCGCCTCCACCCTCGTGCATAACGGAACCTCCGCCAGAGCCACAACCACACCGCT

Tyros #24

L E G F A S P L T G I A D A S Q S S M H N A L H I Y M N G T

CTGGAAGGCTTTGCCTCCCCCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCATGCATAACGCTCTGCATATCTATATGAATGGCACA

RDTLLGPGRPYRAIDFSHQGPAFVTWHRYH
AGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCCGCTTTCGTCACCTGGCACAGATACCAT

TYPOS #1

A M L L A V L Y C L L W S F Q T S A G H F P R A C V S S K
GCCGCTATGCTCCTGGCTGTGCTCTGCTCTGGTCCTTCCAAACCTCCGGCGGACACTTTCCCAGAGCCTGTGTGTCCAGCAAA

gp100 #35
A F E L T V S C Q G G L P K E A C M E I S S P G C Q P P A Q
GCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGGCTTGCATGGAGATTAGCTCCCCCGGATGCCAACCCCCTGCCCAA

Tyros #6

V D D R E S W P S V F Y N R T C Q C S G N F M G F N C G N C

GTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAACTGT

gp100 #34
E S A E I L Q A V P S G E G D A F E L T V S C Q G G L P K E
GAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAA

TRP2 #20 TVCDSLDDYNHLVTLCNGTYEGLLRRNQMG

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ACCGTCTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAAGCAAATGGGA

TYPOS #5

L L S N A P L G P Q F P F T G V D D R E S W P S V F Y N R T

CTGCTCAGCAATGCCCCTCTGGGACCCCCAATTCCCTTTCACAGGCGTCGACGATAGGGAAAGCTGGCCCTCCGTGTTTTACAATAGGACA

MART #8

Y E K L S A E Q S P P P Y S P A A

TACGAAAAGCTCAGCGCTGAGCAAAGCCCTCCCCTTACTCCCCCGCTGCC

9P100 #41
I V G I L L V L M A V V L A S L I Y R R R L M K Q D F S V P
ATCGTCGGCATTCTGCTCGTGCTCATGGCTCTGGCTCAGCCTCATCTATAGGAGAAGGCTCATGAAACAGGATTTCTCCGTGCCT

TYPOS #31
Y S Y L Q D S D P D S F Q D Y I K S Y L E Q A S R I W S W L
TACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTC

MUCIF#6
Q G Q D V T L A P A T E P A S G S A A T W G Q D V T S V P V
CAGGGACAGGATGTGACACTGGCTCCCGCTACCGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTC

9p100 #21

T S C G S S P V P G T T D G H R P T A E A P N T T A G Q V P
ACCTCCTGCGGAAGCTCCCCGGGAACCACAGACGGACACAGACCCCACAGCCCGAAGCCCCTAACACAACCGCTGGCCAAGTGCCT

MUC1R #3
L V H N G T S A R A T T T P A S K S T P F S I P S H H S D T
CTGGTCCACAATGGCACAAGCGCTAGGGCTACCACAACCCCTGCCTCCAAGTCCACCCCTTTCTCCATCCCTAGCCATCACTCCGACACA

TRP2 #32

E E T P G W P T T IL L V V M G T L V A L V G L F V L L A F L GAGGAAACCCCTGGCTGGCCCACAACCCTCCTGGTCGTGATGGGCACACTGGTCGCCCTCGTGGGACTGTTTTGTGCTCCTGGCTTTCCTC

gp100 #29
T T T E W V E T T A R E L P I P E P E G P D A S S I M S T E
ACCACAACCGAATGGGTCGAGACAACCGCTAGGGAACTGCCTATCCCTGAGCGTGGGGACCCGATGCCTCCAGCATTATGTCCACCGAA

MCIR #17
G A V T L T I L L G I F F L C W G P F F L H L T L I V L C P
GGGGTTTGACACTGACAATCCTCCTGGGGAATCTTTTTCCTCTGCTGGGGCCCTTTCTTCTGCACACTGACACTGATTGTGCTCTGCCCT

TYPOS #33

L G A A M V G A V L T A L L A G L V S L L C R H K R K Q L P

CTGGGAGCCGCTATGGTCGGCGCTGTGCTCACCGCTCTGCTCGCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCT

MC1R #8

G A L V A R A A V L Q Q L D N V I D V I T C S S M L S S L C

GGCGCTCTGGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCATCGTGGATTACCTGTAGCTCCATGCTCAGCTCCATGTT

gp100 #26
M T P E K V P V S E V M G T T L A E M S T P E A T G M T P A
ATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGATGGGCACAACCCTCGCCGAAATGTCCACCCCTGAGGCTACCGGAATGACACCCCCCT

MCIR#11
ALRYHSIVTLPRAPRAVAAIWVASVVFSTL
GCCCTCAGGTATCACTCCATCGTCACCCTCCCCAGAGCCCCTAGGGCTGTGGCTGCCATTTGGGTCGCCTCCCGTGGTCTTCTCCACCCCTC

MUC1R  $\sharp 12$  F R E G T I N V H D V E T Q F N Q Y K T E A A S R Y N L T I TTCAGAGAGGGAACCATTAACGTCCACGATGTGGAAACCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACCTCACCATT

Tyros#3
NLMEKECCPPWSGDRSPCGQLSGRGSCQNI

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# 179/216

AACCTCATGGAAAAGGAATGCTGTCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGCTCCTGCCAAAACATT.

Tyros #32
IKSYLEQASRIWSWLLGAAMVGAVLTALLA 

PTT LASHSTKT DASSTHHSSVPPLTSSNHS CCCACAACCCTCGCCTCCCACTCCACCAAAACCGATGCCTCCAGCACACACCATAGCTCCGTGCCTCCCCTCACCTCCAGCAATCACTCC

MUC1R #15 'S G A G V P G W G I A L L V L V C V L V A L A I V Y L I A L AGCGGAGCCGGAGTGCCTGGCTGGGCATTGCCCTCCTGGTCCTGGTCTGGTCCTGGTCCTCGCCATTGTGTATCTGATTGCCCTC

FLGAIAV DRYISIFY ALRYHSIVTLPRAPR TTCCTCGGCGCTATCGCTGTGGATAGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGA

gp100 #40 LIMPGOEAGLGOVPLIVGILLVLMAVVLAS CTGATTATGCCTGGCCAAGAGGCTGGCCTCGGCCAAGTGCCTCTGATTGTGGGAATCCTCCTGGTCCTGATGGCCGTCCTCGCCTCC

T L V A L V G L F V L L A F L Q Y R R L R K G Y T P L M E T ACCCTCGTGGCTCTGGTCGGCCTCTTCGTCCTCGCCCTTTCTGCAATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACA

L I S P N S V F S Q W R V V C D S L E D Y D T L G T L C N S CTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGATAGCCTCGAGGATTACCCTCGGCACACTGTGTAACTCC

L N S T P T A I P Q L G L A A N Q T G A R C L E V S I S D G CTGAATAGCACACCCACAGCCATTCCCCAACTGGGACTGGCTGCCAATCAGACAGGCGCTAGGTGTCTGGAAGTGTCCATCTCCGACGGA

H R P L Q E V Y P E A N A P I G H N R E S Y M V P F I P L Y
CACAGACCCCTCCAGGAAGTGTATCCCGAAGCCAATGCCCCTATCGGACACAATAGGGAAAGCTATATGGTCCCCTTTATCCCTCTGTAT

gp100 #24
EPSGTTSVOVPTTEVISTAP.VQMPTAESTG GAGCCTAGCGGAACCACAAGCGTCCAGGTCCCCACAACCGAAGTGATTAGCACAGCCCCTGTGCAAATGCCTACCGCTGAGTCCACCGGA

K K R V H P D Y V I T T Q H W L G L L G P N G T Q P Q F A N AAGAAAAGGTCCACCCTGACTATGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACACAGCCTCAGTTTGCCAAT

L H Q I L K G G S G T Y C L N V S L A D T N S L A V V S T Q CTGCATCAGATTCTGAAAGGCGGAAGCGGAACCTATTGCCTCAACGTCAGCCTCGCCGATACCAATAGCCTCGCCGTCGTCTCCACCCAA

. PEPEGPDASSIMSTESITGSLGPLLDGTAT 

S I T G S L G P L L D G T A T L R L V K R Q V P L D C V L Y
AGCATTACCGGAAGCCTCGGCCCTCTGCTCGACGGAACCGCTACCCTCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCGTCCTGTAT

gp100 #5 DCWRGGQVSLKVSNDGPTLIGANASFSIAL GACTGTTGGAGAGGCGGACAGGTCAGCCTCAAGGTCAGCAATGACGGACCCACACTGATTGGCGCTAACGCTAGCTTTAGCATTGCCCTC

Synthetic Protein:

wnroly pewteaorldcwrggovslkvsndpy i lrnoddrelwprkffhrtckctgnfagrngdff i sskdlgydysylodsdpdsfodyaa pafltw HRYHLLRLEKDMOEMLOEPSFSGHNRESYMVPFI PLYRNGDFFI SSKDLGYDLLCLERDLQRLIGNESFALPYWNFATGRNETTEVVGTTPGQAPTAE PSGTTSVQVPTTEVSTDYYQELQRDISEMFLQIYKQGGFLGLSNACMEISSPGCQPPAQRLCQPVLPSPACQLVDQLGYSYAIDLPVSVEETPGWPTT LLVVMGTEDGPIRRNPAGNVARPMVQRLPEPQDVAQCMTVDSLVNKECCPRLGAESANVCGSQQGRNQYKTEAASRYNLTISDVSVSDVPFPFSAQAA MSPLWWGFLLSCLGCKILPGAQGQFPRVADLSYTWDFGDSSGTLISRALVVTHTYLEPLAEMSTPEATGMTPAEVSIVVLSGTTAAQVIKFRPGSVVV OLTLAFREGTINVHDVETOFGSAATWGODVTSVPVTRPALGSTTPPAHDVLHKRQRPVHQGFGLKGAVTLTILLGIFFLCLALIICNAIIDPLIYAFH SOELRRTLKEVLKFFHRTCKCTGNFAGYNCGDCKFGWTGPNCLSLQKFDNPPFFQNSTFSFRNALEGFDKADSKSTPFSIPSHHSDTPTTLASHSTKT DASSAANRPALGSTAPPVHNVTSASGSASGSASTCNGTYEGLLRRNQMGRNSMKLPTLKDIRDCTHHSSVPPLTSSNHSTSPQLSTGVSFFFLSFIAY

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#### 180/216

YDHVAVLLCLVVFFLAMLVLMAVLYVKLTGDENFTI PYWDWRDAEKCDI CTDEYMGLRLVKRQVPLDCVLYRYGSFSVTLDI VQGI FLQI YKQGGFLG LSNIKFRPGSVVVQLTLAVIDVITCSSMLSSLCFLGAIAVDRYISIFYRNPGNHDKSRTPRLPSSADVEFCLSLTQYEFDEWLRRYNADISTFPLENA pighnrqynmvsladtnslavvstqlimpgqeaglgqvplgpvtaqvvlqaaipltscgsspvpgttdghkfgfwgpncterrllvrrnifdlsapek DKLGTHTMEVTVYHRRGSRSYVPLAHSSSAFTAVAAIWVASVVFSTLFIAYYDHVAVLLCLVGTLDSQVMSLHNLVHSFLNGTNALPHSAANGCWYCR rrngyralmdkslhvgtqcaltrrpwhrlfllrweqeiqkltgdenftipywdwaamavqgsqrrllgslnstptaipqlglaavvatiaknrnlhsp MYCFICCLALSDLLVSQSSMHNALHIYMNGTMSQVQGSANDPIFLLGQHPTNPNLLSPASFFSSWQIVCSRLEEYNYCFICCLALSDLLVSGTNVLET avillleadptlisrnsrfsswetvcdslddynhlvtltRpalgsttppahdvtsapdnkaardaekcdictdeymggqhptnpnllspasftfalql HDPSGYLAEADLSYTWDFGDSSGTSSADVEFCLSLTQYESGSMDKAANFSFRNTGPTLIGANASFSIALNFPGSQKVLPDGQVIWGPFFLHLTLIVLC PEHPTCGC1FKNFNLFCQCSGNFMGFNCGNCKFGFWGPNCTERRLLQYRRLRKGYTPLMETHLSSKRYTEEAAAPLENAP1GHNRQYNMVPFWPPVTN temfvtnfpgsqkvlpdgqviwvnntiingsqvwggrptaeapnttagqvpttevvgttpgqaptastpggeketsatqrssvpssteknavsmtsli yrrrlmkodfsvpolphssshwlrlprilgilgpngtopofancsvydffvwlhyysvclevglfdtpppysnstnsfrntvegysdpaamdlvlkrc  ${\tt LLHLAVIGALLAVGATKVPRNQTGARCLEVSISDGLFLSLGLVSLVENALSGSMDKAANFSFRNTLEGFASPLTGIADASSPCGQLSGRGSCQNILLS$ NAPLGPQFPFTGMHYYVSMDALLGGSE1WRD1DFAHEAPAFLEEKQPLLMEKEDYHSLYQSHLAAGQCTEVRADTRPWSGPY1LRNQDDRELWPRSVP SSTEKNAVSMTSSVLSSHSPGSGSSTTTPMFNDINIYDLFVWMHYYVSMDALLGGSEQPVYPQETDDACIFPDGGPCPSGSWSQKRSDSLEDYDTLGT LCNSTEDGPIRRNPAGNVAWVNNTIINGSQVWGGQPVYPQETDDACIFPQEKNCEPVVPNAPPAYEKLSAEQSPPPYSPSRSYVPLAHSSSAFTIIDQ VPFSVSVSQLRLEKDMQEMLQEPSFSLPYMNFATGKNVCDIVPFWPPVTNTEMFVTAPDNLGYTYEAACSVYDFFVWLHYYSVRDTLLGPGRPYRAID VRRNIFDLSAPEKDKFFAYLTLAKHTISSDKKGHGHSYTTAEEAAGIGILTVILGVLLLIFVYVWKTWGQYWQVLGGPVSGLSIGTGRAMGGPVSGLS IGTGRAMLGTHTMEVTVYHRRGISTAPVOMPTAESTGMTPEKVPVSEVMGTTFSSWQIVCSRLEEYNSHQSLCNGTPEGPLRDPIFVVLHSFTDAIFD EWMKRFWPPADAWPHMLARACOHAOGIARLHKRORPVHQGFGLKLLTVLTVVTGSGHASSTPGGEKETSATORSFCSCPIGENSPLLSGQQVAATFSF RNALEGFDKADGTLDSOVMSLINLVHSHOSLCNGTPEGPLRRNPGNHDKSRTPRLPPFFPPVTNEELFLTSDQLGYSYAIDLPVSVERKKPPVIRQNI hslspoereofigaldlagelapighnrmynmvpffppvtneelfltsevsivvlsgttaaqvtttewvettarelpitspqlstgvsffflshisn LOFNSSLEDPYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLLFLSLGLVSLVENALVVATIAKNRNLHSPMSFLNGTNALPHSAANDPIFVVLHSFTDA IFAVCQCRRKNYGQLDIFPARDTYHPMSEYPTVFFLAMLVLMAVLYVHMLARACQHAQGIARSTNSFRNTVEGYSDPTGKYDPAVRSLHNLALPYWNF ATGKNVCDICTDDLMGSRSNFDSTITDQVPFSVSVSQLRALDGGNKHFLRNQPLFHISNLQFNSSLEDPSTDYYQELQRDISEMSPYEKVSAGNGGSS LSYTNPAVAAASANLAYVIPIGTYGQMKNGSTPMFNDINIYDLFVWRLCQPVLPSPACQLVLHQILKGGSGTYCLNRYGSFSVTLDIVQGIESAEILQ avpsgegdhhafvdsifeqwlqrhrplqevypeanapictddlmgsrsnfdstlispnsvfsqwrvvcfpardtyhpmseyptyhthgryvppsstdr SYTNPAVAAASANLAAEHPTCGC1FKNFNLFLALI1CNA11DPLIYMSQVQGSANDP1FLLHHAFVDS1FEQWLQRRNSMKLPTLKD1RDCLSLQKFD NPPFFQNSLISRALVVTHTYLEPGPVTAQVVLQAAIPLSFALPYWNFATGRNECDVCTDQLFGAARPDVIGALLAVGATKVPRNQDWLGVSRQLRTKA ALDGGNKHFLRNOPLTFALQLHDPSGYLAECDVCTDQLFGAARPDDPTLISRNSRFSSWÉAAMPREDAHFIYGYPKKGHGHSYTTAEEAATGKYDPAV RSLHNLAHLFLNGTGGQTHLSSSDVSVSDVPFPFSAQSGAGVPGWGIALLVLSPQEREQFLGALDLAKKRVHPDYVITTQHWFFAYLTLAKHTISSDY VIPIGTYGQMKNGSGTNVLETAVILLLEAGALVARAAVLQQLDNVCVLVALAIVYLIALAVCQCRRKNYGQLDICPQEGFDHRDSKVSLQEKNCEFVV PNAPPASVLSSHSPGSGSSTTQGQDVTLAPATEPASDEWMKRFNPPADAWPQELAPIGHNRMYNMVAFHSQELRRTLKEVLTCSWAAFSHQGPAFVTW HRYHLLCLERDLQRLIGNERPMVQRLPEPQDVAQCLEVGLFDTPPFYSNQDPIFVLLHTFTDAVFDEWLRRYNADISTFLGAESANVCGSQQGRGQCTEVRADTRPWSGYNCGDCKFGWTGPNCERKKPPVIRQNIHSLHLFLNGTGGQTHLSSQDPIFVLLHTFTDAVGLVSLLCRHKRKQLPEEKQPLLMEKED YHSGCKI LPGAOGOFPRVCMTVDSLVNKECCPROLPHSSSHWLRLPR I FCSCP I GENSPLLSGDGGPCPSGSWSOKRSFVYVWKTWGOYWOVLNODWL GVSRQLRTKAWNRQLYPEWTEAQRLIWRDIDFAHEAPAFLPWHRLFLLRWEQEIQAAMTPGTQSPFFLLLLLTVLTVVTGSGHASDKSLHVGTQCALT RRCPOEGFDHRDSKVSI NVTSASGSASGSASTI.VHNGTSARATTTPALEGFASPLTGI ADASOSSMHNALHI YMNGTRDTLLGPGRPYRA I DFSHOGP AFVTWHRYHAAMLLAVLYCLLWSFOTSAGHFPRACVSSKAFELTVSCOGGLPKEACMEISSPGCOPPAOVDDRESWPSVFYNRTCOCSGNFMGFNCGN CESAE I LOAVPSGEGDAFELTVSCOGGLPKETVCDSLDDYNHLVTLCNGTYEGLLRRNQMGLLSNAPLGPOFFFTGVDDRESWPSVFYNRTYEKLSAE QSPPPYSPAAIVGILLVLMAVVLASLIYRRRLMKQDFSVPGIGILTVILGVLLLIGCWYCRRRNGYRALMYSYLQDSDPDSFQDYIKSYLEQASRIWS wlqqqdvtlapatepasgsaatwqqdvtsvpvtscgsspvpgttdghrptaeapnttagqvplvhngtsaratttpaskstpfsipshhsdteetpgw PTTLLVVMGTLVALVGLFVLLAFLTTTEWVETTARELP1 PEPEGPDASS IMSTEGAVTLT1 LLG1 FFLCWGPFFLHLTL1 VLCPLGAAMVGAVLTALL AGLVSLLCRHKRKQLPGALVARAAVLQQLDNVIDVITCSSMLSSLCMTPEKVPVSEVMGTTLAEMSTPEATGMTPAQTSAGHFPRACVSSKNLMEKEC CPPWSGDRALRYHSIVTLPRAPRAVAAIWVASVVFSTLFREGTINVHDVETQFNQYKTEAASRYNLTINLMEKECCPPWSGDRSPCGQLSGRGSCQNI IKSYLEQASRIWSWLLGAAMVGAVLTALLAPTTLASHSTKTDASSTHHSSVPPLTSSNHSSGAGVPGWGIALLVLVCVLVALAIVYLIALFLGAIAVD RYISIFYALRYHSIVTLPRAPRLIMPGQEAGLGQVPLIVGILLVLMAVVLASTLVALVGLFVLLAFLQYRRLRKGYTPLMETLISPNSVFSQWRVVCD ${\tt SLEDYDTLGTLCNSLNSTPTAIPQLGLAANQTGARCLEVSISDGHRPLQEVYPEANAPIGHNRESYMVPFIPLYEPSGTTSVQVPTTEVISTAPVQMP$ TAESTGKKRVHPDYVITTQHWLGLLGPNGTQPQFANLHQILKGGSGTYCLNVSLADTNSLAVVSTQPEPEGPDASSIMSTESITGSLGPLLDGTATSI TGSLGPLLDGTATLRLVKRQVPLDCVLYDCWRGGQVSLKVSNDGPTLIGANASFSIAL

#### Synthetic DNA:

TGGAATAGGCAACTGTATCCCGAATGGACAGAGGCTCAGAGACTGGATTGCTGGAGGGGGGGCCAAGTGTCCCTGAAAGTGTCCAACGATCCCTATATTTATCTCCAGCAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACTCCTTCCAAGACTATGCCGCTCCCGCTTTCCTCACCTGG CACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTTCTTCTCCGGCCATAACAGAGAGTCCTACATGGTGCCTTT ATGAGTCCTTCGCTCTGCCTTACTGGAACTTTGCCACAGGCAGAAACGAAACGACACACAGGGTCGTGGGAACCACACCCGGACAGGCTCCCACAGCCGAA CCTCCGGCACAACCTCCGTGCAAGTGCCTACCACAGAGGTCAGCACAGACTATTACCAAGAGGCTCCAGAGAGACATTAGCGAAATGTTTCTGCAAAT CTATAAGCAAGGCGGATTCCTCGGCCTCAGCAATGCCTGTATGGAAATCTCCAGCCCTGGCTGTCAGCCTCCCGCTCAGAGACTGTGTCAGCCTGTGC TCCCCTCCCCGCTTGCCAACTGGTCGACCAACTGGGATACTCCTACGCTATCGATCTGCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACA CTGCTCGTCGTCGTCGTGGAACCGAAGACGGACCCATTAGGAGAAACCCTGCCGGAAACGTCGCCAGACCCATGGTGCAAAGGCTCCCCGAACCCCAAGA GAAACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCTTTCTCCGCCCAAGCCGCT ATGTCCCCCTCTGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCCGGAGCCCAAGGCCAATTCCCTAGGGTCGCCGATCTGTCCTA AAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTCATCAAATTCAGACCCCGGAAGCGTCGTGGTC CAGCTCACCCTCGCCTTTAGGGAAGGCACAATCAATGTGCATGACGTCGAGACACAGTTTGGCTCCGCCGCTACCTGGGGCCAAGACGTCACCTCCGT GCCTGTGACAAGGCCTGCCCTCGGCTCCACCACACCCCCTGCCCATGACGTCCTGCATAAGAGACAGAGACACGAGACCCGTCCAACGAGGCTTTGGCCTCAAGG AGCCAAGAGCTCAGGAGAACCCTCAAGGAAGTGCTCAAGTTTTTCCATAGGACATGCAAATGCACAGGCAATTTCGCTGGCTATAACTGTGGCGATTG 

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GACGCTAGCTCCGCCGCTAACAGACCCGCTCTGGGAAGCACAGCCCCTCCCGTCCACAATGTGACAAGCGCTAGCGGAAGCGCTAGCGGAAGCGCTAG CACATGCAATGGCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGGCAGAAACTCCATGAAACTGCCTACCCTCAAGGATATCAGAGACTGTACCC TACGATCACGTCGCCGTCCTGCCTCGTGGTCTTCTTCTGGCTATGCTCGTGCTCATGGCTGTGCTCTACGTCAAGCTCACCGGAGACGAAAA TCGACTGTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATTTTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGA CTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGTGCAACTGACACTGGCTGTGATTGACGTCACATGCTCCAGCATGCTCCAGCCTGTG CTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTCTATAGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCG CTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAATTCGATGAGTGGCTGAGAAGGTATAACGCTGACATTAGCACATTCCCTCTGGAAAACGCT CGGACTGGGACAGGTCCCCCTCGGCCCTGTGACAGCCCCAGGTGGTCCTGCAAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTTGTGCCTGGCA GACAAACTGGGGACCCATACCATGGAGGTCACCGTCTACCATAGGAGAGGCTCCAGGTCCTACGTCCCCCTCGCCCATAGCTCCAGCGCTTTCACAGC CGTCGCCGCTATCTGCGTGGCTAGCGTCGTGTTTAGCACACTGTTTATCGCTTACTATGACCATGTGGCTGTGCTCCTGTGTCTGGTCGGCACACTGG AGGAGAAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGACCCTGGCACAGACTGTTTCTGCTCAG GTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAATCCCTTACTGGGACTGGGCCGCTATGGCTGTGCAAGGCTCCCAGAGAAGGC TCCTGGGAAGCCTCAACTCCACCCCTACCGCTATCCCTCAGCTCGCCTCGCCGCTGTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCT ATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTGTCCCAGTCCAGCATGCACAATGCCCTCCACATTTACATGAACCGAACCATGAG  ${\tt CCAAGTGCAAGGCTCCGCCAATGACCCTATCTTTCTGCTCGGCCAACACCCTACCAATCCCAATCTCGCTCAGCCCTGCCTTCTTTAGCTCCTGGCCAACACCCTACCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCTCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCAATCA$ AAATCGTCTGCTCCAGGGTCGAGGAATACAATTACTGTTTCATTTGCTGTCTGGCTCTGTCCGACCTCCTGGTCAGCGGAACCAATGTGCTCGAGACA GCCGTCATCCTCCTGCTCGAGGCTGACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGTGACTCCCTGGATGACTATAA CCATCTGGTCACCCTCACCAGACCCGCTCTGGGAAGCACACCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAAGCCGCTAGGGATGCCG AAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCTGTCCCCGCTAGCTTTACCTTTGCCCTCCAGGTC CACGATCCCTCCGGCTATCTGGCTGAGGCTGACCTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACAAGCTCCGCCGATGTGGAATTCTGTCT GTCCCTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACAGGCCCTACCCTCATCGGAGCCAATGCCTCCTTCT CCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATTTGGGGGACCCTTTTTCCTCCACCTCACCCTCATCGTCCTGTGT CCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTTTGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATT CGGATTCTGGGGCCCTAACTGTACCGAAAGGAGACTGCTCCAGTATAGGAGACTGAGAAAGGGATACACACCCCTCATGGAAACCCATCTGTCCAGCA AAAGGTATACCGAAGAGGCTGCCGCTCCCCTCGAGAATGCCCCTTATCGGACACAATAGGCAATACAATATGGTCCCCTTTTTGGCCTCCCGTCACCAAT GTGGGGCGGAAGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACAACCCCTGGCCAAGCCCCTACCG CTAGCACACCCGGAGGCGAAAAGGAAACCTCCGCCACACAGAGAAGCTCCGTGCCTAGCTCCACCGAAAAGAATGCCGTCAGCATGACCTCCCTGATT TACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCACTCCAGCTCCCACTGGCTGAGACTGCCTAGGATTCTGGGACTGCTCGG  $\tt CCCTAACGGAACCCAACTCCCTAACTGTAGCGTCTACGATTTCTTTGTGTGCTCCATTACTATAGCGTCTGCCTCGAGGTCGGCCTCTTCG$ ATACCCCTCCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCTGCCGCTATGGATCTGGTCCTGAAAAGGTGT CTGCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGAAACCGAACCGGAGCCAGATGCCTCGAGGTCAGCATTAG CGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGTCGAGAATGCCCTCAGCGGAAGCATGGACAAAGCCGCTAACTTTAGCTTTAGGAATACCC TCGAGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCCAGCCCTTGCGGACAGCTCAGCGGAAGGGGAAGCTGTCAGAATATCCTCCTGTCC AACGCTCCCCTCGGCCCTCAGTTTCCCCTTTACCGGAATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGAGACATTGA CTTTGCCCATGAGGCTCCCGCTTTCCTCGAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCCG TCCAGCACAGAGAAAAACGCTGTGTCCATGACAAGCTCCGTGCTCAGCTCCCACCCGGAAGCGGAAGCTCCACCACAACCCCTATGTTTAACGA TATCAATATCTATGACCTCTTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAACAGCCTGTGTATCCCCAAGAGACAG CTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCTTGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGG AGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCTCAGGAAAAGAATTGCGAACCCGTCGTGCCTAACGCTCCCCCTGCCTATG AGAAACTGTCCGCCGAACAGTCCCCCCCTCCCTATAGCCCTAGCAGAAGCTATGTGCCTCTGGCTCAGCTCCGCCTTTACCATTACCGATCAG GTCCCCTTTAGCGTCAGCGTCAGCCAACTGAGACTGGAAAAGGATATGCAAGAGATGCTGCAAGAGCCTAGCTTTAGCCTCCCCTATTGGAATTTCGC TACCGGAAAGAATGTGTGTGACATTGTGCCTTTCTGGCCCCCTGTGACAAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATG AGGCTGCTGCTCCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACACTGCTCGGCCCTGGCAGACCCTATAGGGCTATCGAT AAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGCAGAGCCATGGGCGGACCCGTCAGCGGACTGTCC ATCGGAACCGGAAGGGCTATGCTCGGCACACACACAATGGAAGTGACAGTGTATCACAGAAGGGGAATCTCCACCGCTCCCGTCCAGATGCCCACAGC ATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGAGACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGAT GAGTGGATGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCTCACATGCTGGCTAGGGCTTGCCAACACGCTCAGGGAATCGCTAGGCTCCACAAAAG GCAAAGGCCTGTGCATCAGGGATTCGGACTGAAACTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGACACGCTAGCTCCACCCTTGGCGGAGAGA AAGAGACAAGCGCTACCCAAAGGTCCTTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCTACCTTTAGCTTT AGGAATGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCATAGCCATCAGTCCCTGTGTAA CACTCCCTGTCCCCCAAGAGAGAGAGCAATTCCTCGGCGCTCTGGATCTGGCTCAGGAACTGGCTCCCATTGGCCATAACAGAATGTATAACATGGT GCCTTTCTTTCCCCCTGTGACAAACGAAGAGCTCTTCCTCACCTCCGAGGTCAGCATTGTGGTCCTGTCCGGCACAACCGCTGCCCAAGTGACAACCA CAGAGTGGGTGGAAACCACAGCCAGAGAGCTCCCCCATTACCTCCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGCTTTCACATTAGCAAT CTGCAATTCAATAGCTCCCTGGAAGACCCTTACCATACCCATGGCAGATACGTCCCCCCTAGCTCCACCGATAGGTCCCCCTATGAGAAAGTGTCCGC CGGAAACGGAGGCTCCAGCCTCCTGTTTCTGTCCCTGGGACTGGTCAGCCTCGTGGAAAACGCTCTGGTCGTGGCTACCATTGCCAAAAACAGAAAACC TCCACTCCCCATGAGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCCGCCGCTAACGATCCCATTTTCGTCGTGCTCCACTCCTTCACAGACGCT ATCTTTGCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACAGT GTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCATATGCTCGCCAGAGCCTGTCAGCATGCCCAAGGCATTGCCAGAAGCACAAACT

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 $\tt CCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCTCTACTGGAACTTT$ GCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACAATCACAGACCAAGTGCCTTTCTCCGT TCGAGGATCCCTCCACCGATTACTATCAGGAACTGCAAAGGGATATCTCCGAGATGAGCCCTTACGAAAAGGTCAGCGCTGGCAATGGCGGAAGCTCC CTGTCCTACACAAACCCTGCCGTCGCCGCTGCCTCCGCCAATCTGGCTTACGTCATCCCTATCGGAACCTATGGCCAAATGAAAAACGGAAGCACACC TCAAGGGAGGCTCCGGCACATACTGTCTGAATAGGTATGGCTCCTTCTCCGTGACACTGGATATCGTCCAGGGAATCGAAAGCGCTGAGATTCTGCAA GCCGTCCCTCCGGCGAAGGCGATCACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCATAGGCCTCTGCAAGAGGTCTACCCTGA GGCTAACGCTCCCATTTGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCAATAGCGTCTTCTCCCAGTGGAGGG AGCTATACCAATCCCGCTGTGGCTGCCGCTAGCGCTAACCTCGCCGCTGAGCATCCCACATGCGGATGCATTTTCAAAAACTTTAACCTCTTCCTCGC TCGACTCCATCTTTGAGCAATGGCTCCAGAGAAGGAATAGCATGAAGCTCCCCACACTGAAAGACATTAGGGATTGCCTCAGCCTCCAGAAATTCGAT AACCCTCCTTTTTCCAAAACTCCCTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGCTCAGGTCGTGCTCCA GACCCGATGTGATTGGCGCTCTGCTCGCCGTCGGCGCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT GCCCTCGACGGAGGCAATAAGCATTTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCCTAGCGGATACCTCGCCGAATGCGATGT GTGTACCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAAGCCGCTATGCCTAGGG AAGACGCTCACTTTATCTATGGCTATCCCAAAAAGGGACACGGACACTCCTACACAACCGCTGAGGAAGCCGCTACCGGAAAGTATGACCCTGCCGTC TCGCCAAAAAGGAGTGCATCCCGATTACGTCATCACAACCCAACACTGGTTCTTTGCCTATCTGACACTGGCTAAGGATACCATTAGCTCCGACTAT GTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCCGGCACAAACGTCCTGGAAACCGCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGT GAAAGAATTACGGACAGCTCGACATTTGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTC CCCAATGCCCTCCCGCTAGCGTCCTGTCCAGCCATAGCCCTGGCTCCGGCTCCAGCACAACCCAAGGCCAAGACGTCACCCTCGCCCTGCCACAGA GCCTGCCTCCGACGAATGGATGAAGAGATTCAATCCCCCTGCCGATGCCTGGCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGG TCGCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCCTTCTCCCACCAAGGCCCTGCCTTTGTGACATGG TCAGTGTCTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAATCAGGATCCCATTTTCGTCCTGCTCCACACATTCACAGACGCTGTGTTTG ACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTTCTGGGAGCCGAAAGCGCTAACGTCTGCGGAAGCCAACAGGGAAGGGGACAGTGTACC GAAGTGAGAGCCGATACCAGACCCTGGAGCGGATACAATTGCGGAGACTGTAAGTTTGGCTGGACCGGACCCAATTGCGAAAGGGAAAAAGCCTCCCGT CATCAGACAGAATATCCATAGCCTCCACCTCTTCCTCAACGGAACCGGAGGCCAAACCCATCTGTCCAGCCAAGACCCTATCTTTGTGCTCCTGCATA CCTTTACCGATGCCGTCGGCCTCGTGTCCCTGCTCTGCAGACACAAAAGGAAACAGCTCCCCGAAGAGAAACAGCCTCTGCTCATGGAAAAGGAAGAC TATCACTCCGGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAGCCTCGTGAATAAGGAATGCTGTCCCAG ACAGCTCCCCATAGCTCCAGCCATTGGCTCAGGCTCCCCAGAATCTTTTGCTCCTGCCCTATCGGAGAGAATAGCCCTCTGCTCAGCGGAGACGGAG GCCCTTGCCCTAGCGGAAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGACAGTATTGGCAAGTGCTCAACCAAGACTGGCTG TCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGAAATCCAAGCCGCTATGACACCCGGAACCCAAAGCCCTT TCTTTCTGCTCCTGCTCCTGACAGTGCTCACCGTCGTGACAGGCTCCGGCCATGCCTCCGACAAAAGCCTCCACGTCGGCACACAGTGTGCCCTCACC AGAAGGTGTCCCCAAGAGGGGATTCGATCACAGAGACTCCAAGGTCAGCCTCAACGTCACCTCCGGCTCCGGCTCCGGCTCCGGCTCCGCCTCCACCCT CGTGCATAACGGAACCTCCGCCAGAGCCACAACCACACCCGCTCTGGAAGGCTTTGCCTCCCCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCA TGCATAACGCTCTGCATATCTATATGAATGGCACAAGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCC AGCCTGTGTGTCCAGCAAAGCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGCTTGCATGGAGATTAGCTCCCCGGATGCCAAC TGTGAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAAACCGT CTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAACCAAATGGGACTGCTCAGCAATG GAAACAGGATTTCTCCGTGCCTGGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTCGTCATCGGATGCTGGTACTGTAGGAGAAGGAATGGCT ATAGGGCTCTGATGTACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCC TGGCTCCAGGGACAGGATGTGACACTGGCTCCCGCTACCGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTCAC CCCACAACCCTCCTGGTCGTGATGGGCACACTGGTCGCCCTCGTGGGACTGTTTGTGCTCCTGGCTTTCCTCACCACAACCGAATGGGTCGAGACAAC CGCTAGGGAACTGCCTATCCCTGAGGCCTGAGGGACCCGATGCCTCCAGCATTATGTCCACCGAAGGCGCTGTGACACTGACAATCCTCCTGGGAATCT TTTTCCTCTGCTGGGGCCCTTTCTTTCTGCATCTGACACTGATTGTGCTCTGCCCTCTGGGAGCCGCTATGGTCGGCGCTGTGCTCACCGCTCTGCTC GCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCTGGCGCTCTGGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCAT CGATGTGATTACCTGTAGCTCCATGCTCAGCTCCCTGTGTATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGATGGGCACAACCCTCGCCGAAATGT CCACCCCTGAGGCTACCGGAATGACACCCGCTCAGACAAGCGCTGGCCATTTCCCTAGGGCTTGCGTCAGCTCCAAGAATCTGATGGAGAAAGAGTGT TGCCCTCCTGGAGCGGAGACAGAGCCCTCAGGTATCACTCCATCGTCACCCTCCCCAGAGCCCCTAGGGCTGTGGCTGCCATTTGGGTCGCCTCCGT GGTCTTCTCCACCCTCTTCAGAGAGGGAACCATTAACGTCCACGATGTGGAAACCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACC TCACCATTAACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGGCTCCTGCCAAAACATT ATCAAAAGCTATCTGGAACAGGCTAGCAGAATCTGGAGCTGCTCGCGGGGCTGCCATGGTGGGAGCCGTCCTGACAGCCCTCCTGGCTCCCACAAC TTCTGCAATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACACTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGAT AGCCTCGAGGATTACGATACCCTCGGCACACTGTGTAACTCCCTGAATAGCACACCCCACAGCCATTCCCCAACTGGGACTGGCTGCCAATCAGACAGC 

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ATATGGTCCCCTTTATCCCTCTGTATGAGCCTAGCGGAACCACAAGCGTCCAGGTCCCACAACCGAAGTGATTAGCACAGCCCCTGTGCAAATGCCT
ACCGCTGAGTCCACCGGAAAGAAAAGGGTCCACCTGACTATGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACACAGCCTCA
GTTTGCCAATCTGCATCAGATTCTGAAAGGCGGAACCTATTGCCTTAACGTCAGCCTCGCCGATACCAATAGCCTCGCCGTCGTGTCCACCC
AACCCGAACCCGAAGGCCCTGACGCTAGCTCCATCATGAGCACAGGATCCATCACAGGCTCCCTGGGACCCCTCCTGGATGGCACAGCCACAAGCATT
ACCGGAAGCCTCGCCCTTGCTTCGACGGAACCGCTACCCTCAGGGTCGTGAAAAGGCAAGTGCCTCTGGATTGCGTCCTGTATGACTGTTGGAGGG
CGGACAGGTCAGCCTCAAGGTCAGCAATGACGACCCACACTGATTGGCGCTCAACGCTTAGCATTTGCCTCC

Melanoma cancer Specific Savine Scramble process Scramble - Output File Scramble version : 0.1 beta, 08/02/1999 Num. genes Num. segments Segment length : 30 Segment overlap : 15 Segments in original order: : BAGE Segment# : 1 Offset 1st Codon : 1 A A M A A R A V F L A L S A Q L L Q A R L M K E E S P V V S : BAGE Segment# : 2 Offset : 16 1st Codon : 1 L L Q A R L M K E E S P V V S W R L E P E D G T A L C F I F CTGCTCCAGGCTAGGCTCATGAAAGAGGAAAGCCCTGTGGTCAGCTGGAGGCTCGAGGCTGGAGGATGGCACAGCCCTCTGCTTTATCTTT Gene : BAGE Segment# : 3 / Offset : 31 1st Codon : 1 WRLEPEDGTALCFIFAA TGGAGACTGGAACCCGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCC : GAGE-1. Segment# : 1 1st Codon : 1 A A M S W R G R S T Y R P R P R R Y V E P P E M I G P M R P GCCGCTATGTCCTGGAGAGGCAGAAGCACATACAGACCCAGACCCAGAAGGTATGTGGAACCCCTGAGATGATCGGACCCATGAGGCCT : GAGE-1 Gene Segment# : 2 Offset 1st Codon : 1 RRYVEPPEMIGPMRPEQFSDEVEPATPEEG AGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGACCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGGA: GAGE-1 Gene Segment# : 3 Offset : 31 1st Codon : 1 EQFSDEVEPATPEEGEPATQRQDPAAAQEG GAGCAATTCTCCGACGAAGTGGAACCCGCTACCCCTGAGGAAGGCGAACCCGCTACCCAAGAGCCAAGACCCCTGCCCAAGAGGGA : GAGE-1 Gene Segment# : 4 Offset 1st Codon : 1 E P A T Q R Q D P A A A Q E G E D E G A S A G Q G P K P E A GAGCCTGCCACACAGAGACAGGATCCCGCTGCCGCTCAGGAAGGCGAAGACGAAGGCGCTAGCGCTGGCCCAAGGCCCTAAGCCTGAGGCT : GAGE-1 Segment# : 5 Offset : 61 1st Codon : 1

Figure 27 (Cont)

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E D E G A S A G Q G P K P E A D S Q E Q G H P Q T G C E C E GAGGATGAGGGAGCCTCCGCCGGACAGGGACCCAAACCCGAAGCCGATAGCCAAGAGCAAGAGCCATCCCCAAACCGGATGCGAATGCGAA : GAGE-1 Segment# : 6 Offset 1st Codon: 1
DSQEQGHPQTGCECEDGPDGQEMDPPNPEE GACTCCCAGGAACAGGGACACCCTCAGACAGGCTGTGAGTGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAA Gene : GAGE-1 Segment# : 7 Offset : 91 1st Codon : 1 D G P D G Q E M D P P N P E E V K T P E E E M R S H Y V A Q GACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGTCAAGACACCCGAAGAGAGAAATGAGAAGCCATTACGTCGCCCAA Gene : GAGE-1 Segment# : 8 Offset : 106 V K T P E E E M R S H Y V A Q T G I L W L L M N N C F L N L GTGAAAACCCCTGAGGAAGAGATGAGGTCCCACTATGTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTC Gene : GAGE-1 Segment# : 9 Offset : 121 lst Codon: 1
TGILWLLMNNCFLNLSPRKPAA ACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCT : gp100In4 Gene Segment# : 1 Offset 1st Codon : 1 A A S W S Q K R S F V Y V W K T W G E G L P S Q P I I H T C  ${\tt GCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGGAAGACATGGGGAGAGGGACTGCCTAGCCAACCCATTATCCATACCTGT}$ : gp100In4 Segment# : 2 Offset : 16 1st Codon : 1 T W G E G L P S O P I I H T C V Y F F L P D H L S F G R P F Gene : gp100In4 Segment# : 3 Offset : 31 1st Codon : 1 V Y F F L P D H L S F G R P F H L N F C D F L A A GTGTATTTCTTTCTGCCTGACCATCTGTCCTTCGGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCC : MAGE-1 Gene Segment# : 1 A A M S L E Q R S L H C K P E E A L E A Q Q E A L G L V C V GCCGCTATGTCCCTGGAACAGAGAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGCTCAGCAAGAGGCTCTGGGACTGGTCTGCGTC : MAGE-1 Segment# : 2 Offset : 16 EALEAQQEALGLVCVQAATSSSSPLVLGTL Gene : MAGE-1 Segment# : 3 Offset : 31 1st Codon: 1 O A A T S S S S P L V L G T L E E V P T A G S T D P P Q S P CAGGCTGCCACAAGCTCCAGCTCCCCCCTCGTGCTCGGCACACTGGAAGAGGTCCCCACAGCCGGGAAGCACAGACCCTCCCCAAAGCCCT

Figure 27 (Cont)

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: MAGE-1 Gene Segment# : 4 Offset 1st Codon : 1 Segment# : 5 Offset : 61 1st Codon : 1 Q G A S A F P T T I N F T R Q R Q P S E G S S S R E E E G P : MAGE-1 Gene Segment# : 6 : 76 1st Codon: 1
R Q P S E G S S S R E E E G P S T S C I L E S L F R A V I T AGGCAACCCTCCGAGGGAAGCTCCAGCAGAGAGGAAGAGGGACCCTCCACCTCCTGCATTCTGGAAAGCCTCTTCAGAGCCGTCATCACA : MAGE-1 Segment# : 7 : 91 1st Codon : 1 S T S C I L E S L F R A V I T K K V A D L V G F L L L K Y R AGCACAAGCTGTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTGAAATACAGA Gene : MAGE-1 Segment# : 8 : 106 Offset 1st Codon: 1 KKVADLVGFLLLKYRAREPVTKAEMLESVI AAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAGTCCGTGATT Gene Segment# : 9 Offset GCCAGAGAGCCTGTGACAAAGGCTGAGATGCTGGAAAGCGTCATCAAAAACTATAAGCATTGCTTTCCCGAAATCTTTGGCAAAGCCTCC : MAGE-1 Segment# : 10 Offset : 136 1st Codon : 1 K N Y K H C F P E I F G K A S E S L Q L V F G I D V K E A D AAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTAGCGAAAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGAT : MAGE-1 Gene Segment# : 11 : 151 Offset GAGTCCCTGCAACTGGTCTTCGGAATCGATGTGAAAGAGGCTGACCCTACCGGACACTCCTACGTCCTGGTCACCTGTCTGGGACTGTCC : MAGE-1 Gene Segment# : 12 : 166 Offset 1st Codon : 1
 P T G H S Y V L V T C L G L S Y D G L L G D N Q I M P K T G : MAGE-1 Gene Segment# : 13 : 181 Offset 1st Codon : 1 Y D G L L G D N Q I M P K T G F L I I V L V M I A M E G G H Gene : MAGE-1

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Segment# : 14 Offset : 196 1st Codon: 1
FLIIVLV MIAMEGGHAPEEEIWEELS V MEV : MAGE-1 Gene Segment# : 15 Offset : 211 1st Codon : 1 A PEEEL SVMEVYDGREHSAYGEPRKL GCCCTGAGGAAGAGATTTGGGAAGAGCTCAGCGTCATGGAAGTGTATGACGGAAGGGAACACTCCGCCTATGGCGAACCCAGAAAGCTC : MAGE-1 Gene Segment# : 16 : 226 Offset 1st Codon: 1
Y D G R E H S A Y G E P R K L L T Q D L V Q E K Y L E Y R Q
Y D G R E H S A Y G E P R K L L T Q D L V Q E K Y L E Y R Q TACGATGGCAGAGAGCATAGCGCTTACGGAGAGCCTAGGAAACTGCTCACCCAAGACCTCGTGCAAGAAAATACCTCGAGTATAGGCAA : MAGE-1 Gene Segment# : 17 Offset 1st Codon : 1 L T Q D L V Q E K Y L E Y R Q V P D S D P A R Y E F L W G P : MAGE-1 Segment# : 18 Offset : 256 1st Codon : 1 V P D S D P A R Y E F L W G P R A L A E T S Y V K V L E Y V GTGCCTGACTCCGACCCTGCCAGATACGAATTCCTCTGGGGACCCAGAGCCCTCGCCGAAACCTCCTACGTCAAGGTCCTGGAATACGTC : MAGE-1 Gene Segment# : 19 Offset 1st Codon : 1 R A L A E T S Y V K V L E Y V I K V S A R V R F F F P S L R : MAGE-1 Segment# : 20 : 286 Offset I K V S A R V R F F P S L R E A A L R E E E G V A A ATCAAAGTGTCCGCCAGAGTGAGATTCTTTTTCCCTAGCCTCAGGGAAGCCGCTCTGAGAGAGGGAAGAGGAAGGCGTCGCCGCT Gene : MAGE-3 Segment# : 1 Offset 1st Codon : 1 LEQRSQHCKPEEGLEARGÉALGLVGA GCCGCTATGCCTCTGGAACAGAGAAGACCAACACTGTAAGCCTGAGGAAGGCCTCGAGGGTAGGGGGAGAGGCTCTGGGACTGGTCGGCGCT : MAGE-3 Gene Segment# : 2 Offset EGLEARGEALGLVGAQAPATEEQEAASSS GAGGGACTGGAAGCCAGAGGCGAAGCCCTCGGCCTCGTGGGAGCCCCAAGCCCCTGCCACAGAGGAACAGGAAGCCGCTAGCTCCAGCTCC : MAGE-3 Segment# : 3 : 31 Offset 1st Codon : 1 Q A P A T E E Q E A A S S S T L V E V T L G E V P A A : MAGE-3 Gene Segment# : 4

Figure 27 (Cont)

Offset

: 46

```
1st Codon: 1
T L V E V T L G E V P A A E S P D P P Q S P Q G A S S L P T
ACCCTCGTGGAAGTGACACTGGGAGAGGTCCCCGCTGCCGAAAGCCCTGACCCTCCCAAAGCCCTCAGGGAGCCTCCAGCCTCCCCACA
        : MAGE-3
Segment# : 5
Offset
        : 61
 P D P P Q S P Q G A S S L P T T M N Y P L W S Q S Y E D S S
: MAGE-3
Segment# : 6
Offset
        : 76
T M N Y P L W S Q S Y E D S S N Q E E E G P S T F P D L E S
ACCATGAACTATCCCCTCTGGTCCCAGTCCTACGAAGACTCCAGCAATCAGGAAGAGGAGGAGGCCCTAGCACATTCCCTGACCTCGAGTCC
        : MAGE-3
Segment# : 7
Offset
        : 91
1st Codon : 1
N Q E E E G P S T F P D L E S E F Q A A L S R K V A E L V H
AACCAAGAGGAAGAGGGACCCTCCACCTTTCCCGATCTGGAAAGCGAATTCCAAGCCGCTCTGTCCAGGAAAGTGGCTGAGCTCGTGCAT
Gene
        : MAGE-3
Segment# : 8
Offset
        : 106
1st Codon: 1
EFQAALSRKVAELVHFLLLKYRAREPVTKA
GAGTTTCAGGCTGCCCTCAGCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGCCAGAGAGCCTGTGACAAAGGCT
        : MAGE-3
Gene
Segment# : 9
       : 121 /
Offset
1st Codon : 1
F L L L K Y R A R E P V T K A E M L G S V V G N W Q Y F F P TTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGGCTCCGTGGTCGGCAATTGCCAATGCTTTTTCCCT
        : MAGE-3
Segment# : 10
Offset : 136
1st Codon : 1
EMLGS V V G N W Q Y F F P V I F S K A S S S L Q L V F G
: MAGE-3
Gene
Segment# : 11
        : 151
Offset
1st Codon: 1
V I F S K A S S S L Q L V F G I E L M E V D P I G H L Y I F
GTGATTTTCTCCAAGGCTAGCTCCAGCCTCCAGCTCGTGTTTGGCATTGAGCTCATGGAAGTGGATCCCATTGGCCATCTGTATATCTTT
       : MAGE-3
Gene
Segment# : 12
       : 166
Offset
1st Codon : 1
I E L M E V D P I G H L Y I F A T C L G L S Y D G L L G D N
ATCGAACTGATGGAGGTCGACCCTATCGGACACCTCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAAT
        : MAGE-3
Gene
Segment# : 13
A T C L G L S Y D G L L G D N Q I M P K A G L L I I V L A I
GCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATT
        : MAGE-3
Segment# : 14
Offset
       : 196
1st Codon : 1
Q I M P K A G L L I I V L A I I A R E G D C A P E E K I W E
```

Figure 27 (Cont)

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CAGATTATGCCTAAGGCTGGCCTCCTGATTATCGTCCTGGCTATCATTGCCAGAGAGGGGAGACTGTGCCCCTGAGGAAAAGATTTGGGAA
        : MAGE-3
Gene
Segment#
        : 15
Offset
        : 211
1st Codon : 1
 I A R E G D C A P E E K I W E E L S V L E V F E G R E D S I
: MAGE-3
Gene
Segment# : 16
Offset
        : 226
1st Codon : 1
 ELS V L E V F E G R E D S I L G D P K K L L T Q H F V Q E
GAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAA
        : MAGE-3
Gene
Segment# : 17
Offset
        : 241
1st Codon : 1
 L G D P K K L L T Q H F V Q E N Y L E Y R Q V P G S D P A C
: MAGE-3
Segment# : 18
Offset
        : 256
1st Codon : 1
N Y L E Y R Q V P G S D P A C Y E F L W G P R A L V E T S Y
\textbf{AACTATCTGGAATACAGACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTAT}
Gene
        : MAGE-3
Segment#
        : 19
Offset
        : 271
1st Codon : 1
 Y E F L W G P R A L V E T S Y V K V L H H M V K I S G G P H
TACGAATTCCTCTGGGGACCCAGAGCCCTCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCAT
        : MAGE-3
Gene
       : 20
Segment#
Offset
        : 286
1st Codon : 1
V K V L H H M V K I S G G P H I S Y P P L H E W V L R E G E GTGAAAGTGCTCCACCATATGGTCAAGATTAGCGAGGCCCTCACATTAGCTATCCCCCTCTGCATGAGTGGGTGCTCAGGGAAGGCGAA
Gene
        : MAGE-3
Segment# : 21
Offset
       : 301
1st Codon : 1
I S Y P P L H E W V L R E G E E A A
ATCTCCTACCCTCCCCCCCACGAATGGGTCCTGAGAGGGGAGAGGGAAGCCGCT
        : PRAME
Gene
Segment#
       : 1
Offset
1st Codon : 1
A A M E R R R L W G S I Q S R Y I S M S V W T S P R R L V E
GCCGCTATGGAAAGGAGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGTCCGTGTGGACCTCCCCCAGAAGGCTCGTGGAA
        : PRAME
Gene
Segment# : 2
Offset
       : 16
1st Codon : 1
Y I S M S V W T S P R R L V E L A G Q S L L K D E A L A I A
TACATTAGCATGAGCGTCTGGACAAGCCCTAGGAGACTGGTCGAGCTCGCCGGACAGTCCCTGCTCAAGGATGAGGCTCTGGCTATCGCT
        : PRAME
```

LAGQSLLKDEALAIAALELLPRELFPPLFM CTGGCTGGCCAAAGCCTCCTGAAAGACGAAGCCCTCGCCATTGCCGCTCTGGAACTGCTCCCCAGAGAGCTCTTCCCTCTCCTCATG

Segment# : 3 1st Codon : 1

#### 189/216

: PRAME Gene Segment# : 4 : 46 Offset 1st Codon : 1 A L E L L P R E L F P P L F M A A F D G R H S Q T L K A M V

: PRAME Gene Segment# : 5 Offset : 61

1st Codon: 1
A A F D G R H S Q T L K A M V Q A W P F T C L P L G V L M K GCCGCTTTCGATGGCAGACACTCCCAGACACTGAAAGCCATGGTGCAAGCCTGGCCCTTTACCTGTCTGCCTCTGGGAGTGCTCATGAAA

: PRAME Gene Segment# : 6 Offset : 76 1st Codon : 1

Q A W P F T C L P L G V L M K G Q H L H L E T F K A V L D G CAGGCTTGGCCTTTCACATGCCTCCCCTCGGCGTCCTGATGAAGGGACAGCATCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGA

: PRAME Segment# : 7 Offset 1st Codon : 1

G Q H L H L E T F K A V·L D G L D V L L A Q E V R P R R W K GGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCGACGTCCTGGTCGCCCAAGAGGTCAGGCCTAGGAGATGGAAA

: PRAME Segment# : 8 Offset : 106 lst Codon : 1

LDVLLAQEVRPRRWKLQVLDLRKNSHQDFW 

: PRAME Gene Segment# : 9 Offset : 121 1st Codon : 1

L Q V L D L R K N S H Q D F W T V W S G N R A S L Y S F P E CTGCAAGTGCTCGACCTCAGGAAAAACTCCCACCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAA

: PRAME Gene Segment# : 10

T V W S G N R A S L Y S F P E P E A A Q P M T K K R K V D G ACCGTCTGGTCCGGCAATAGGGCTAGCCTCTACTCCTTCCCTGAGCCTGAGGCTGCCCAACCCATGACCAAAAAGGGAAAGGTCGACGGA

: PRAME Segment# : 11 Offset : 151 1st Codon : 1

PEAAQPM T K K R K V D G L S T E A E Q P F I P V E V L  $\tt CCCGAAGCCGCTCAGCCTATGACAAAGAAAAGGAAAGTGGATGGCCTCAGCACAGAGGCTGAGCAACCCTTTATCCCTGTGGAAGTGCTC$ 

Gene : PRAME
Segment# : 12 Offset : 166

1st Codon: 1 LSTEAEOPFIPVEVLVDLFLKEGACDELFS 

: PRAME Gene Segment# : 13 Offset : 181

1st Codon: 1
V D L F L K E G A C D E L F S Y L I E K V K R K K N V L R L  ${\tt GTGGATCTGTTTCTGAAAGAGGGAGCCTGTGACGAACTGTTTAGCTATCTGATTGAGAAAGTGAAAAAGGAAAAGGAAAAGGAATGTGCTCAGGCTC}$ 

: PRAME Gene Segment# : 14

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```
Offset
       : 196
1st Codon : 1
 Y L I E K V K R K K N V L R L C C K K L K I F A M P M Q D I
TACCTCATCGAAAAGGTCAAGAGAAAAGAAAAAACGTCCTGAGACTGTGTTGCAAAAAGCTCAAGATTTTCGCTATGCCTATGCCAAGACATT
Gene
        : PRAME
       : 15
Segment#
Offset
        : 211
1st Codon: 1
C C K K L K I F A M P M Q D I K M I L K M V Q L D S I E D L
TGCTGTAAGAAACTGAAAATCTTTGCCATGCCCATGCAGGATATCAAAATGATTCTGAAAATGGTCCAGCTCGACTCCATCGAAGACCTC
        : PRAME
Gene
Segment# : 16
        : 226
Offset
1st Codon : 1
 K M I L K M V Q L D S I E D L E V T C T W K L P T L A K F S
AAGATGATCCTCAAGATGCTGCAACTGGATAGCATTGAGGATCTGGAAGTGACATGCACATGGAAACTGCCTACCCTCGCCAAATTCTCC
Segment#
       : 17
Offset
1st Codon : 1
E V T C T W K L P T L A K F S P Y L G Q M I N L R R L L L S
GAGGTCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCC
        : PRAME
Segment# : 18
        : 256
Offset
1st Codon : 1
PYLGOMINLR RLLLSHIHASSYISPEKEEQ
CCCTATCTGGGACAGATGATCAATCTGAGAAGGCTCCTGCTCAGCCATATCCATGCCTCCAGCTATATCTCCCCCGAAAAGGAAGAGCAA
        : PRAME
Gene
Segment#
       : 19
        : 271
Offset
HIHASSYISPEKEEQYIAQFTSQFLSLQCL
CACATTCACGCTAGCTCCTACATTAGCCCTGAGAAAGAGGGAACAGTATATCGCTCAGTTTACCTCCCAGTTTCTGTCCCTGCAATGCCTC
        : PRAME
Segment#
       : 20
Offset
        : 286
YIAQFTSQFLSLQCLQALYVDSLFFLRGRL
TACATTGCCCAATTCACAAGCCAATTCCTCAGCCTCCAGTGTCTGCAAGCCCTCTACGTCGACTCCCTGTTTTTCCTCAGGGGAAGGCTC
Gene
        : PRAME
Segment# : 21
        : 301
Offset
1st Codon: 1
O A L Y V D S L F F L R G R L D Q L L R H V M N P L E T L S
CAGGCTCTGTATGTGGATAGCCTCTTCTTCTGAGAGGGCAGACTGGATCAGCTCCTGAGACACGTCATGAATCCCCTCGAGACACTGTCC
        : PRAME
Gene
       : 22
Segment#
        : 316
Offset
1st Codon : 1
D Q L L R H V M N P L E T L S I T N C R L S E G D V M H
GACCAACTGCTCAGGCATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGAGACGTCATGCATCTGTCC
        : PRAME
Segment# : 23
        : 331
1st Codon : 1
 I T N C R L S E G D V M H L S Q S P S V S Q L S V L S L S G
ATCACAAACTGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTAGCGTCAGCCAACTGTCCGTGCTCAGCCTCAGCGGA
Gene
        : PRAME
Segment#
       : 24
Offset
        : 346
1st Codon : 1
```

Figure 27 (Cont)

```
Q S P S V S Q L S V L S L S G V M L T D V S P E P L Q A L L
 CAGTCCCCTCCGTGTCCCAGCTCAGCGTCCTGTCCCTGTCCGGCGTCATGCTCACCGATGTGTCCCCCGAACCCCTCCAGGCTCTGCTC
                    : PRAME
 Segment# : 25
 Offset
                   : 361
1st Codon : 1
V M L T D V S P E P L Q A L L E R A S A T L Q D L V F D E C
 GTGATGCTGACAGACGTCAGCCCTGGAGCCTCTGCAAGCCCTCCTGGAAAGGGCTACCCTCCAGGATCTGGTCTTCGATGAGTGT
                    : PRAME
 Gene
 Segment# : 26
 Offset
                  : 376
 1st Codon : 1
  ERASATLQDLVFDECGITDDQLLALLPSLS
GAGAGAGCCTCCGCCACACTGCAAGACCTCGTGTTTGACGAATGCGGAATCACAGACGATCAGCTCCTGGCTCTGCTCCCTGTCC
                    : PRAME
Segment# : 27
                   : 391
Offset
 1st Codon : 1
  G I T D D Q L L A L L P S L S H C S Q L T T L S F Y G N S I
GGCATTACCGATGACCAACTGCTCGCCCTCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACACTGTCCTTCTATGGCAATAGCATT
                   : PRAME
Gene
Segment# : 28
                  : 406
Offset
1st Codon : 1
H C S Q L T T L S F Y G N S I S I S A L Q S L L Q H L I G L CACTGTAGCCAACTGCACCTCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCTCCAGTCCCTGCTCCAGCATCTGATTGGCCTC
                   : PRAME
Segment# : 29
Offset : 421
1st Codon : 1
S I S A L Q S L L Q H L I G L S N L T H V L Y P V P L E S Y AGCATTAGCGCTCTGCAAAGCCTCATCGGACGCTGTCCAACCCTCATCGGACGCTGTCCCAACCCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTAT
Gene
                   : PRAME
Segment# : 30
Offset
                  : 436
1st Codon: 1
S N L T H V L Y P V P L E S Y E D I H G T L H L E R L A Y L
AGCAATCTGACACGTCCTGTATCCCGTCCCCCTCGAGTCCTACGAAGACATTCACGGAACCCTCCACCTCGAGAGACTGGCTTACCTC
                   : PRAME
Gene
Segment# : 31
Offset : 451
1st Codon: 1
E D I H G T L H L E R L A Y L H A R L R E L L C E L G R P S
GAGGATATCCATGGCACACTGCATCTGGAAAGGCTCGCCTATCTGCATGCCAGACTGAGAGAGGCTCCTGTGTGAGCTCGGCAGACCCTCC
Gene
                  : PRAME
Segment# : 32
Offset
                 : 466
1st Codon : 1
 HARLRELLCELGRPSMVWLSANPCPHCGDR
{\tt CACGCTAGGCTCAGGGAACTGCTCTGCGAACTGGGAAGGCCTAGCATGGTGTGGCTGTCCGCCAATCCCTGTCCCCATTGCGGAGACAGA}
                   : PRAME
Gene
Segment# : 33
                  : 481
Offset
1st Codon : 1
 M V W L S A N P C P H C G D R T F Y D P E P I L C P C F M P
{\tt ATGGTCTGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCCTTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATGCTATG
                   : PRAME
Gene
Segment# : 34
                 : 496
Offset
1st Codon : 1
 TFYDPEPILCPCFMPNAA
ACCTTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCT
```

Figure 27 (Cont)

WO 01/090197

```
· TRP2TN2
Gene
Segment# : 1
Offset
1st Codon: 1
A A L M E T H L S S K R Y T E E A G G F F P W L K V Y Y Y R
GCCGCTCTGATGGAGACACCCTCAGCTCCAAGAGATACACAGAGGAAGCCGGAGGCTTTTTCCCTTGGCTCAAGGTCTACTATTACAGA
Gene
        : TRP2IN2
       : 2
Segment#
        : 16
Offset
1st Codon : 1
 E A G G F F P W L K V Y Y Y R F V I G L R V W Q W E V I S C
GAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTGTGATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGT
        : TRP2IN2
Gene
Segment# : 3
        : 31
Offset
1st Codon : 1
F V I G L R V W Q W E V I S C K L I K R A T T R Q P A A
TTCGTCATCGGACTGAGAGTGTGGCAGTGGGAGGTCATCTCCTGCAAACTGATTAAGAGAGCCACAACCAGACAGCCTGCCGCT
Gene
Segment#
A A M Q A E G R G T G G S T G D A D G P G G P G I P D G P G
GCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGATGCCGATGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGA
         : NYNSO1a
Segment#
        : 2
Offset
        : 16
1st Codon : 1
DADGPGGPGIIPDGPGGNAGGPGEAGATGGR
GACGCTGACGCACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGCTACCGGAGGCAGA
        : NYNSOla
Gene
Segment#
        : 3
Offset
G N A G G P G E A G A T G G R G P R G A G A A R A S G P G G
GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGGACCCAGAGGCGCTGGCGCTGCCAGAGCCTCCGGCCCTGGCGGA
        : NYNSOla
Segment#
       : 4
        : 46
Offset
G P R G A G A R A S G P G G G A P R G P H G G A A S G L N
GGCCCTAGGGGAGCCGCTAGGGCTAGCGCACCCGGAGCCGGAGCCCCTAGGGGACCCCATGGCGAGCCGCTAGCGGACTGAAT
        : NYNSO1a
Gene
Segment#
       : 5
Offset
        : 61
1st Codon : 1
G A P R G P H G G A A S G L N G C C R C G A R G P E S R L L
GGCGCTCCCAGAGGCCCTCACGGAGGCGCTGCCTCCGGCCTCAACGGATGCTGTAGGTGTGGCGCTAGGGGACCCGAAAGCAGACTGCTC
        : NYNSOla
Gene
Segment#
        : 6
Offset
G C C R C G A R G P E S R L L E F Y L A M P F A T P M E A E
GGCTGTTGCAGATGCGGAGCCAGAGGCCCTGAGTCCAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAA
        : NYNSOla
Segment#
        : 7
        : 91
Offset
1st Codon : 1
E F Y L A M P F A T P M E A E L A R R S L A Q D A P P L P V
GAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAGGCTGAGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCCTCCCCGTC
Gene
        : NYNSOla
```

Figure 27 (Cont)

```
Segment# : 8
        : 106
Offset
1st Codon : 1
 L A R R S L A Q D A P P L P V P G V L L K E F T V S G N I L
\tt CTGGCTAGGAGAAGCCTCGCCCAAGACGCTCCCCCTCTGCCTGGCGTGCCTGGCGTCAAGGAATTCACAGTGTCCGGCAATATCCTC
        : NYNSOla
Gene
Segment# : 9
Offset
        : 121
1st Codon : 1
 PGVLLKEFTVSGNILTIRLTAADHRQLQLS
{\tt CCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC}
        : NYNSOla
Segment# : 10
Offset
        : 136
1st Codon : 1
 T I R L T A A D H R Q L Q L S I S S C L Q Q L S L L M W I T
ACCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCATTAGCTCCTGCCTCCAGCAACTGTCCCTGCTCATGTGGATCACA
        : NYNSOla
Gene
Segment# : 11
: NYNSOla
Segment# : 12
Offset
       : 166
1st Codon : 1
 Q C F L P V F L A Q P P S G Q R R A A
CAGTGTTTCCTCCCCGTCTTCCTCGCCCAACCCCCTAGCGGACAGAGAAGGGCTGCC
        : NYNSO1b
Gene
Segment# : 1
Offset
1st Codon : 1
A A M L M A Q E A L A F L M A Q G A M L A A Q E R R V P R A
GCCGCTATGCTCATGGCTCAGGAAGCCCTCGCCTTTCTGATGGCCCAAGGCGCTATGCTCGCCGCTCAGGAAAGGAGAGTGCCTAGGGCT
Gene
        : NYNSO1b
Segment# : 2
Q G A M L A A Q E R R V P R A A E V P G A Q G Q Q G P R G R
CAGGGAGCCATGCTGGCTGCCCAAGAGAGAGAGGGTCCCCAGAGCCGCTGAGGTCCCCGGAGCCCAAGAGGCCAACAGGGACCCAGAGGCAGA
        : NYNSO1b
Gene
Segment# : 3
       : 31
Offset
1st Codon: 1
A E V P G A Q G Q Q G P R G R E E A P R G V R M A A R L Q G
GCCGAAGTGCCTGGCGCTCAGGGACAGCCAAGGCCCTAGGGGAAGGGAAGAGGCTCCCAGAGGCGTCAGGATGGCCGCTAGGCTCCAGGGA
        : NYNSO1b
Gene
Segment# : 4
Offset
lst Codon: 1
E E A P R G V R M A A R L Q G A A
GAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGCTGCC
        : LAGE1
Gene
Segment#
       : 1
Offset
1st Codon : 1
A A M Q A E G Q G T G G S T G D A D G P G G P G I P D G P G
GCCGCTATGCAAGCCGAAGGCCAAGGCACAGGCGGAAGCACAGGCGGATGCCGATGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGA
Gene
        : LAGE1
Segment# : 2
Offset
```

Figure 27 (Cont)

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1st Codon : 1 DADGPGGPGIPDGPGGNAGGPGEAGATGGR GACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGTACCGGAGAGCAGA : LAGE1 Gene Segment# : 3 Offset : 31 1st Codon : 1 G N A G G P G E A G A T G G R G P R G A G A A R A S G P R G GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGACCCAGAGGCGCTGGCGCTGCCAGAGCCTCCGGCCCTAGGGGA Segment# : 4 1st Codon : 1 G P R G A G A A R A S G P R G G A P R G P H G G A A S A Q D GGCCCTAGGGGAGCCGGCTAGGGCTAGCGGACCCAGAGGCGGAGCCCCTAGGGGAACCCCATGGCGGAGCCGCTAGCGCTCAGGAT Segment# : 5 Offset : 61 1st Codon : 1 G A P R G P H G G A A S A Q D G R C P C G A R R P D S R L L GGGCCTCCAGAGGCCCTCACGGAGGCGCTGCCTCCGCCCAAGACGGAAGGTGTCCCTGTGGCGCTAGGAGACCCGATAGCAGACTGCTC Gene : LAGE1 : 6 Segment# Offset : 76 1st Codon : 1 PCGARRPDSRLLQLHITMPFSSPMEAE GGCAGATGCCCTTGCGGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTCTCCAGCCCTATGGAAGCCGAA Gene : 7 Segment# Offset 1st Codon : 1 Q L H I T M P F S S P M E A E L V R R I L S R D A A P L P R Gene : LAGE1 Segment# : 8 Offset : 106 1st Codon: 1 L V R R I L S R D A A P L P R P G A V L K D F T V S G N L L CTGGTCAGGAGAATCCTCAGCAGAGACGCTGCCCCTCTGCCTAGGCCTGGCGCTGTGCTCAAGGATTTCACAGTGTCCGGCAATCTGCTC Gene : LAGE1 Segment# : 9 Offset P G A V L K D F T V S G N L L F I R L T A A D H R Q L Q L S CCCGGAGCCGTCCTGAAAGACTTTACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC : LAGE1 Segment# : 10 Offset : 136 1st Codon : 1 FIRLTAADHRQLQLSISSCLQQLSLLMWIT TTCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCATTAGCTCCTGCCTCCAGCAACTGTCCCTGCTCATGTGGATCACA Gene : LAGE1 Segment# : 11 Offset : 151 1st Codon : 1 I S S C L Q Q L S L L M W I T Q C F L P V F L A Q A P S G Q : LAGE1 Gene Segment# : 12 Offset : 166 1st Codon : 1

Figure 27 (Cont)

Q C F L P V F L A Q A P S G Q R R A A

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CAGTGTTTCCTCCCCGTCTTCCTCGCCCAAGCCCCTAGCGGACAGAGAAGGGCTGCC

Segments in scrambled order:

MAGE-1 #15

A P E E E I W E E L S V M E V Y D G R E H S A Y G E P R K L GCCCCTGAGGAAGAGATTTGGGAAGAGCTCAGCGTCATGGAAGTGTATGACGGAAGGGAACACTCCGCCTATGGCGAACCCAGAAAGCTC

MAGE-1 #4

E E V P T A G S T D P P Q S P Q G A S A F P T T I N F T R Q 

T V W S G N R A S L Y S F P E P E A A Q P M T K K R K V D G ACCGTCTGGTCCGGCAATAGGGCTAGCCTCTACTCCTTCCCTGAGCCTGAGCTGCCCAACCCATGACCAAAAAAGAGAAAGGTCGACGA

MAGE-3 #14

Q I M P K A G L L I I V L A I I A R E G D C A P E E K I W E CAGATTATGCCTAAGGCTGGCCTCCTGATTATCGTCCTGGCTATCATTGCCAGAGAGGGGAGACTGTGCCCCTGAGGAAAAGATTTGGGAA

L Q V L D L R K N S H Q D F W T V W S G N R A S L Y S F P E CTGCAAGTGCTCGACCTCAGGAAAAACTCCCACCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAA

LDVLLAQEVRPRRWKLQVLDLRKNSHQDFW 

Q G A M L A A Q E R R V P R A A E V P G A Q G Q G P R G R 

PRAME #24
OSPSVSQLSVLSLSGVMLTDVSPEPLQALL CAGTCCCCTCCGTGTCCCAGCTCAGCGTCCTGTCCCTGTCCGGCGTCATGCTCACCGATGTGTCCCCCGAACCCCTCCAGGCTCTGCTC

LTQDLVQEKYLEYRQVPDSDPARYEFLWGP 

R Q P S E G S S S R E E E G P S T S C I L E S L F R A V I T 

A A M A A R A V F L A L S A Q L L Q A R L M K E E S P V V S 

PRAME #34
TFYDPEPILCPCFMPNAA ACCTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCT

MAGE-3 #12
I E L M E V D P I G H L Y I F A T C L G L S Y D G L L G D N ATCGAACTGATGGAGGTCGACCCTATCGGACACCTCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAAT

GAGE-1#2
RRYVEPPEMIGPMRPEQFSDEVEPATPEEG AGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGACCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGA

EAGGFFPWLKVYYY RFVIGLRVW QWEVISC GAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTTGTGATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGT

A A M E R R R L W G S I Q S R Y I S M S V W T S P R R L V E GCCGCTATGGAAAGGAGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGTCCGTGTGGACCTCCCCCAGAAGGCTCGTGGAA

A A L M E T H L S S K R Y T E E A G G F F P W L K V Y Y Y R GCCGCTCTGATGGAGACACACCTCAGCTCCAAGAGATACACAGAGGAAGCCGGAGGCTTTTTCCCTTGGCTCAAGGTCTACTATTACAGA

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A A M S L E Q R S L H C K P E E A L E A Q Q E A L G L V C V GCCGCTATGTCCCTGGAACAGAGAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGCTCAGCAAGAGGCTCTGGGACTGGTCTGCGTC

Q A A T S S S P L V L G T L E E V P T A G S T D P P Q S P CAGGCTGCCACAAGCTCCAGCTCCCCCTCGTGCTCGGCACACTGGAAGAGGTCCCCACAGCCGGAAGCACAGACCCTCCCCAAAGCCCT

A L E L L P R E L F P P L F M A A F D G R H S Q T L K A M V GCCCTCGAGCTCCTGCCTAGGGAACTGTTTCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCAAACCCTCAAGGCTATGGTC

ELSVLEVFEGREDSILGDPKKLLTQHFVQE GAGCTCAGCGTCCTGGAGTGTTTGAGGGAAGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAA

ESLQLVFGIDVKEADPTGHSYVLVTCLGLS GAGTCCCTGCAACTGGTCTTCGGAATCGATGTGAAAGAGGCTGACCCTACCGGACACTCCTACGTCCTGGTCACCTGTCTGGGACTGTCC

MAGE-3 #5
PDPPQSPQGASSLPTTMNYPLWSOSYEDSS CCCGATCCCCTCAGTCCCCCCAAGGCGCTAGCTCCCTGCCTACCACAATGAATTACCCTCTGTGGAGCCAAAGCTATGAGGATAGCTCC

A A M Q A E G Q G T G G S T G D A D G P G G P G I P D G P G GCCGCTATGCAAGCCGAAGGCCAAGGCACAGGCGGAAGCACAGGCGGATGCCGATGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGA

NYNSO1a #12 Q C F L P V F L A Q P P S G Q R R A A 

T W G E G L P S Q P I I H T C V Y F F L P D H L S F G R P F ACCTGGGGCGAAGGCCTCCCCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCAGCTTTGGCAGACCCTTT

T S C I L E S L F R A V I T K K V A D L V G F L L K Y R AGCACAAGCTGTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTGAAATACAGA

GCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGGATGCCGATGGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGA

D G P D G Q E M D P P N P E E V K T P E E E M R S H Y V A O GACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGTCAAGACCCCGAAGAGAGAAATGAGAAGCCATTACGTCGCCCAA

NYNS01a #11

E R A S A T L Q D L V F D E C G I T D D Q L L A L L P S L S GAGAGAGCCTCCGCCACACTGCAAGACCTCGTGTTTGACGAATGCGGAATCACAGACGATCAGCTCCTGGCTCTGCTCCCTGCTCC

LGDPKKLLTQHFVQENYLEYRQVPGSDPAC 

E A L E A Q Q E A L G L V C V Q A A T S S S S P L V L G T L GAGGCTCTGGAAGCCCAACAGGAAGCCCTCGGCCTCGTGTGTGCAAGCCGCTACCTCCAGCTCCAGCCCTCTGGTCCTGGGAACCCTC

E F Y L A M P F A T P M E A E L A R R S L A Q D A P P L P V GAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAGGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCTCCCCGTC

E E A P R G V R M A A R L Q G A A GAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGCTGCC

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BAGE #3
WRLEPEDGTALCFIFAA TGGAGACTGGAACCCGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCC

GAGE-1 #3
E Q F S D E V E P A T P E E G E P A T Q R Q D P A A A Q E G GAGCAATTCTCCGACGAAGTGGAACCCGCTACCCTGAGGAAGGCGAACCCGCTACCCAAAGGCAAGACCCTGCCGCTGCCCAAGAGGGA

MAGE-3 #6
T M N Y P L W S Q S Y E D S S N Q E E E G P S T F P D L E S ACCATGAACTATCCCCTCTGGTCCCAGGAGAGACTCCAGCAATCAGGAAGAGGCCCTAGCACATTCCCTGACCTCGAGTCC

MAGE-3 #7
NQEEEGPSTFPDLESEFQAALSRKVAELVH AACCAAGAGGAAGAGGGACCCTCCACCTTTCCCGATCTGGAAAGCGAATTCCAAGCCGCTCTGTCCAGGAAAGTGGCTGAGCTCGTGCAT

PRAME #13
V D L F L K E G A C D E L F S Y L I E K V K R K K N V L R L GTGGATCTGTTTCTGAAAGAGGGAGCCTGTGACGAACTGTTTAGCTATCTGATTGAGAAAGTGAAAAGGAAAAAGAATGTGCTCAGGCTC

NYNSOla #10

TIRLTAADHR QLQLSISSCLQQLSLLM WIT ACCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCATTAGCTCCTGCCTCCAGCAACTGTCCCTGCTCATGTGGATCACA

MAGE-3 #1

A A M P L E Q R S Q H C K P E E G L E A R G E A L G L V G A GCCGCTATGCCTCTGGAACAGAGAAGCCAACACTGTAAGCCTGAGGAAGGCCTCGAGGCTAGGGGAGAGGCTCTGGGACTGGTCGGCGCT

D A D G P G G P G I P D G P G G N A G G P G E A G A T G G R GACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGCTACCGGAGGCAGA

MAGE-3 #19

YEFLWGPRALVETSYVKVLHHMVKISGGPH TACGAATTCCTCTGGGGACCCAGAGCCCTCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCAT

ITNCRLSEGDVMHLSOSPSVSOLSVLSLSG ATCACAAACTGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTAGCGTCAGCCAACTGTCCGTGCTCAGCCTCAGCGGA

N Y L E Y R Q V P G S D P A C Y E F L W G P R A L V E T S Y AACTATCTGGAATACAGACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTAT

V I F S K A S S S L Q L V F G I E L M E V D P I G H L Y I F GTGATTTTCTCCAAGGCTAGCTCCAGCCTCCAGCTCGTGTTTGGCATTGAGCTCATGGAAGTGGATCCCATTGGCCATCTGTATATCTTT

PRAME #21

Q A L Y V D S L F F L R G R L D Q L L R H V M N P L E T L S 

Y I A Q F T S Q F L S L Q C L Q A L Y V D S L F F L R G R L TACATTGCCCAATTCACAAGCCAATTCCTCAGCCTCCAGTGTCTGCAAGCCCTCTACGTCGACTCCCTGTTTTTCCTCAGGGGAAGGCTC

G Q H L H L E T F K A V L D G L D V L L A Q E V R P R R W K GGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCGACGTCCTGCCCCAAGAGGGTCAGGCCTAGGAGATGGAAA

LAGE1 #10
FIRLT A A D H R Q L Q L S I S S C L Q Q L S L L M W I T TTCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCATTAGCTCCTGCCTCCAGCAACTGTCCCTGCTCATGTGGATCACA

PRAME #15
CCKKLKIFAMPMQDIKMILKMVQLDSIEDL TGCTGTAAGAAACTGAAAATCTTTGCCATGCCCATGCAGGATATCAAAATGATTCTGAAAATGGTCCAGCTCGACTCCATCGAAGACCTC

NYNSOla #5

G A P R G P H G G A A S G L N G C C R C G A R G P E S R L L GCGCTCCCAGAGGCCCTCACGGAGGCGCTGCCTCCGGCCTCAACGGATGCTGTAGGTGTGGCGCTAGGGGACCCGAAAGCAGACTGCTC

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MAGE-1 #8 K K V A D L V G F L L K Y R A R E P V T K A E M L E S V I AAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAGTCCGTGATT

Y D G L L G D N Q I M P K T G F L I I V L V M I A M E G G H 

SISALOSLLQHLIGLSNLTHVLYPVPLESY AGCATTAGCGCTCTGCAAGCCTCCTGCAACACCTCATCGGACTGTCCAACCTCACCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTAT

I A R E G D C A P E E K I W E E L S V L E V F E G R E D S I ATCGCTAGGGAAGGCGATTGCGCTCCCGAAGAGAAAATCTGGGAGGAACTGTCCGTGCTCGAGGTCTTCGAAGGCAGAGAGGATAGCATT

D Q L L R H V M N P L E T L S I T N C R L S E G D V M H L S GACCAACTGCTCAGGCATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGAGACGTCATGCATCTGTCC

RALAETSYVKVLEYVIKVSARVRFFPSLR 

PRAME #30
S N L T H V L Y P V P L E S Y E D I H G T L H L E R L A Y L AGCAATCTGACACACGTCCTGTATCCCGTCCCCCTCGAGTCCTACGAAGACATTCACGGAACCCTCCACCTCGAGAGACTGGCTTACCTC

AAMLMAQEALAFLMAQGAMLAAQERRVPRA GCCGCTATGCTCATGGCTCAGGAAGCCCTCGCCTTTCTGATGGCCCAAGGCGCTATGCTCGCCGCTCAGGAAAGGAGAGTGCCTAGGGCT

KNYKHCFPEIFGKASESLQLVFGIDVKEAD AAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTAGCGAAAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGAT

PRAME #25
V M L T D V S P E P L Q A L L E R A S A T L Q D L V F D E C GTGATGCTGACAGACGTCAGCCCTGGAGCCCTCGCAAGCCCTCCTGGAAAGGGCTAGCGCTACCCTCCAGGATCTGGTCTTCGATGAGTGT

E D E G A S A G Q G P K P E A D S Q E Q G H P Q T G C E C E CAGGATGAGGGAGCCTCCGCCGGACAGGGACCCAAACCCGAAGCCGATGCCAAGAGAAGGCCATCCCCAAACCGGATGCGAATGCGAA

EMLGSVVGNWQYFFPVIFSKASSSLQLVFG 

A A M S W R G R S T Y R P R P R R Y V E P P E M I G P M R P GCCGCTATGTCCTGGAGAGGCAGAAGCACATACAGACCCAGAACCCAGAAGGTATGTGGAACCCCTGAGATGATCGGACCCATGAGGCCCT

Y I S M S V W T S P R R L V E L A G Q S L L K D E A L A I A TACATTAGCATGAGCGTCTGGACAAGCCCTAGGAGACTGGTCGAGCTCGCCGGACAGTCCCTGCTCAAGGATGAGGCTCTGGCTATCGCT

Y D G R E H S A Y G E P R K L L T Q D L V Q E K Y L E Y R Q TACGATGCAGAGACATAGCGCTTACGGAGAGCCTAGGGAAACTGCTCACGAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAA

Q C F L P V F L A Q A P S G Q R R A A CAGTGTTTCCTCCCCGTCTTCCTCGCCCAAGCCCCTAGCGGACAGAGAAGGGCTGCC

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MAGE-3 #20 V K V L H H M V K I S G P H I S Y P P L H E W V L R E G E ' GTGAAAGTGCTCCACCATATGGTCAAGATTAGCGGAGGCCCTCACATTAGCTATCCCCCTCTGCATGAGTGGGTGCTCAGGGAAGGCGAA Q L H I T M P F S S P M E A E L V R R I L S R D A A P L P R CAGCTCCACATTACCATGCCCTTTAGCTCCCCCATGGAGGCTGAGCTCGTGAGAAGGATTCTGTCCAGGGATGCCGCTCCCCTCCCCAGA P G V L L K E F T V S G N I L T I R L T A A D H R Q L Q L S  ${\tt CCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAACTGCCAACTGTCC}$ K M I L K M V Q L D S I E D L E V T C T W K L P T L A K F S AAGATGATCCTCAAGATGGTGCAACTGGATAGCATTGAGGATCTGGAAGTGACATGCACATGGAAACTGCCTACCCTCGCCAAATTCTCC F L I I V L V M I A M E G G H A P E E E I W E E L S V M E V EVTCTWKLPTLAKFSPYLGQMINLRRLLLS GAGGTCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCC MAGE-3 #2
E G L E A R G E A L G L V G A Q A P A T E E Q E A A S S S S GAGGGACTGGAAGCCGAGGCCTCGTGGGAGCCCTAGCTCCAGCTCCCAGAGGAACAGGAAGCCGCTAGCTCCAGCTCC MAGE-3 #21
ISYPPLHEWVLREGEEAA ATCTCCTACCCTCCACGAATGGGTCCTGAGAGAGGGAGAGGGAAGCCGCT PRAME #19 HIHASSYISPEKEEQYIAQFTSQFLSLQCL G N A G G P G E A G A T G G R G P R G A G A A R A S G P G G GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGACCCAGAGGCGCTGGCGTGCCAGAGGCCTCCGGCCCTGGCGGA G P R G A G A A R A S G P G G A P R G P H G G A A S G L N GGCCCTAGGGGAGCCGGAGCCGCTAGGGGACCCGGAGGCGGAGCCCCTAGGGGACCCCATGGCGGAGCCGCTAGCGGACTGAAT MAGE-1 #5
Q G A S A F P T T I N F T R Q R Q P S E G S S R E E E G P NYNSO1a#8
LARRSLAQDAPPLPVPGVLLKEFTVSGNIL CTGGCTAGGAGAAGCCTCGCCCAAGACGCTCCCCCTCTGCCTGTGCCTGGCGTCCTGCTCAAGGAATTCACAGTGTCCGGCAATATCCTC A A F D G R H S Q T L K A M V Q A W P F T C L P L G V L M K GCCGCTTTCGATGGCAGACACTCCCAGACACTGAAAGCCATGGTGCAAGCCTGGCCCTTTACCTGTCTGCCTCTGGGAGTGCTCATGAAA MAGE-1 #20 I K V S A R V R F F F P S L R E A A L R E E E G V A A ATCAAAGTGTCCGCCAGAGTGAGATTCTTTTTCCCTAGCCTCAGGGAAGCCGCTCTGAGAGAGGGAAGAGGGAAGGCGTCGCCGCT PRAME #27
G I T D D Q L L A L L P S L S H C S Q L T T L S F Y G N S I GGCATTACCGATGACCAACTGCTCGCCTCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACCACTGTCCTTCTATGGCAATAGCATT GAGE-1#8
VKTPEEEMRSHYVAQTGILWLLMNNCFLNL GTGAAAACCCCTGAGGAAGAGAGAGGTCCCACTATGTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTC

Figure 27 (Cont)

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PRAME #14
Y L I E K V K R K K N V L R L C C K K L K I F A M P M Q D I TACCTCATCGAAAAGGTCAAGAGAAAAAACGTCCTGAGACTGTGTTGCAAAAAGCTCAAGATTTTCGCTATGCCTATGCAAGACATT

A R E P V T K A E M L E S V I K N Y K H C F P E I F G K A S GCCAGAGAGCCTGTGACAAAGGCTGAGATGCTGGAAAGCGTCATCAAAAACTATAAGCATTGCTTTCCCGAAATCTTTGGCAAAGCCTCC

LVRRILSRDAAPLPRPGAVLKDFTVSGNLL CTGGTCAGGAGAATCCTCAGCAGAGACGCTGCCCCTCTGCCTAGGCCTGGCGCTGTGCTCAAGGATTTCACAGTGTCCGGCAATCTGCTC

H C S Q L T T L S F Y G N S I S I S A L Q S L L Q H L I G L CACTGTAGCCAACTGACAACCCTCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCTCCAGTCCCTGCTCCAGCATCTGATTGGCCTC

MVWLSANPCPHCGDRTFYDPEPILCPCFMP ATGGTCTGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTTATGCCT

gp100In4 #1
AAS WS QKRS FVYV WKT WG EGLPS QPII HT C GCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGAGAGGGGACTGCCTAGCCAACCCATTATCCATACCTGT

L L Q A R L M K E E S P V V S W R L E P E D G T A L C F I F  $\tt CTGCTCCAGGCTAGGCTCATGAAAGAGGAAAGCCCTGTGGTCAGCTGGAGGCTCGAGCCTGAGGATGGCACAGCCCTCTGCTTTATCTTT$ 

gp100In4 #3
VYFFLPDHLSFGRPFHLNFCDFLAA GTGTATTTCTTCTGCCTGACCATCTGTCCTTCGGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCC

MAGE-3#3
QAPATEEQEAASSSSTLVEVTLGEVPAAES 

QAWPFTCLPLGVLMKGQHLHLETFKAVLDG CAGGCTTGGCCTTTCACATGCCTCCCCCTCGGCGTCCTGATGAAGGGACAGCATCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGA

LSTEAEOPFIPVEVLVDLFLKEGACDELFS 

A E V P G A Q G Q Q G P R G R E E A P R G V R M A A R L Q G GCCGAAGTGCCTGGCGCTCAGGGACAGGCCCTAGGGGAAGGGGAAGGGGAAGGGCTCCCAGAGGCGTCAGGATGGCCCCTAGGCTCCAGGGA

GGGGTCCCAGAGGCCCTCACGGAGGCGCTGCCTCCGCCCAAGACGGAAGGTGTCCCTGTGGCGCTAGGAGACCCGATAGCAGACTGCTC

G P R G A G A A R A S G P R G G A P R G P H G G A A S A Q D GGCCCTAGGGGAGCCGGAGCCGCTAGGGGTAGCGGACCCAGAGGCGGAGCCCCTAGGGGACCCCATGGCGGAGCCGCTAGCGCTCAGGAT

LAGQSLLKDEALAIAALELLPRELFPPLFM CTGGCTGGCCAAAGCCTCCTGAAAGACGAAGCCCTCGCCATTGCCGCTCTGGAACTGCTCCCCAGAGAGCTCTTCCCCCCTCTTCATG

GAGE-1 #4
EPATQRQDPAAAQEGEDEGASAGQGPKPEA GAGCCTGCCACACAGAGACAGGATCCCGCTGCCGCTCAGGAAGGCGAAGACGAAGGCGCTAGCGCTGGCCAAGGCCCTAAGCCTGAGGCT

PEAAQPMTKKRKVDGLSTEAEQPFIPVEVL CCCGAAGCCGCTCAGCCTATGACAAAGAAAAGGAAAGTGGATGGCCTCAGCACAGAGGCTGAGCAACCCTTTATCCCTGTGGAAGTGCTC

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LAGE1 #6 G R C P C G A R P D S R L L Q L H I T M P F S S P M E A E GGCAGATGCCCTTGCGGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTTCTCCAGCCCTATGGAAGCCGAA

PGAVLK D F T V S G N L L F I R L T A A D H R Q L Q L S CCCGGAGCCGTCCTGAAAGACTTTACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCCAACTGTCC

EDINGTLHLERLAYLHARLRELLCELGRPS GAGGATATCCATGGCACACTGCATCTGGAAAGGCTCGCCTATCTGCATGCCAGACTGAGAGAGGCTCCTGTGTGAGCTCGGCAGACCCTCC

GAGE-1 #6
D S Q E Q G H P Q T G C E C E D G P D G Q E M D P P N P E E GACTCCCAGGAACAGGGACACCCTCAGACAGGCTGTGAGTGTGAGGTTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAA

F V I G L R V W O W E V I S C K L I K R A T T R Q P A A TTCGTCATCGGACTGAGAGTGTGGCAGTGGGAGGTCATCTCCTGCAAACTGATTAAGAGAGCCCACAACCAGACAGCCTGCCGCT

D A D G P G G P G I P D G P G G N A G G P G E A G A T G G R GACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGCTACCGGAGGGCAGA

MAGE-1 #12

P T G H S Y V L V T C L G L S Y D G L L G D N Q I M P K T G CCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCAAAACCGGA

F L L L K Y R A R E P V T K A E M L G S V V G N W Q Y F F P TTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGGCTCCGTGGTCGGCAATTGGCAATACTTTTTCCCT

TGILWLLMNNCFLNLSPRKPAA ACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCT

E F Q A A L S R K V A E L V H F L L K Y R A R E P V T K A GAGTTTCAGGCTGCCCTCAGCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGCCAGAGAGCCTGTGACAAAGGCT

MAGE-1 #18

V P D S D P A R Y E F L W G P R A L A E T S Y V K V L E Y V GTGCCTGACTCCGACCCTGCCAGATACGAATTCCTCTGGGGACCCAGAGCCCTCGCCGAAACCTCCTACGTCAAGGTCCTGGAATACGTC

G C C R C G A R G P E S R L L E F Y L A M P F A T P M E A E GGCTGTTGCAGATGCGGAGCCAGAGGCCCTGAGTCCAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAA

ATCLGLSYDGLLGDNQIMPKAGLLIIVLAI GCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATT

G N A G G P G E A G A T G G R G P R G A G A A R A S G P R G GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGAACCCAGAGGCGCTGGCGTGCCAGAGCCTCCGGCCCTAGGGGA

#### Artificial Protein:

apeeeiweelsvmevydgrehsaygeprkleevptagstdppqspqgasafpttinftrqtvwsgnraslysfpepeaaqpmtkkrkvdgqimpkagl LIIVLAIIAREGDCAPEEKIWELQVLDLRKNSHQDFWTVWSGNRASLYSFPELDVLLAQEVRPRRWKLQVLDLRKNSHQDFWQGAMLAAQERRVPRAA EVPGAOGOOGPRGROSPSVSQLSVLSLSGVMLTDVSPEPLQALLLTQDLVQEKYLEYRQVPDSDPARYEFLWGPRQPSEGSSSREEEGPSTSCILESL FRAVITAAMAARAVFLALSAQLLQARLMKEESPVVSTFYDPEPILCPCFMPNAAIELMEVDPIGHLYIFATCLGLSYDGLLGDNRRYVEPPEMIGPMR PEOFSDEVEPATPEEGEAGGFFPWLKVYYYRFVIGLRVWQWEVISCAAMERRRLWGSIQSRYISMSVWTSPRRLVEAALMETHLSSKRYTEEAGGFFP WLKVYYYRAAMSLEORSLHCKPEEALEAQOEALGLVCVQAATSSSSPLVLGTLEEVPTAGSTDPPQSPALELLPRELFPPLFMAAFDGRHSQTLKAMV ELSVLEVFEGREDSILGDPKKLLTQHFVQEESLQLVFGIDVKEADPTGHSYVLVTCLGLSPDPPQSPQGASSLPTTMNYPLWSQSYEDSSAAMQAEGQ GTGGSTGDADGPGGPG1PDGPGOCFLPVFLAQPPSGQRRAATWGEGLPSQP1IHTCVYFFLPDHLSFGRPFSTSCILESLFRAVITKKVADLVGFLLL KYRAAMOAEGRGTGGSTGDADGPGGPGIPDGPGDGPDGQEMDPPNPEEVKTPEEEMRSHYVAQISSCLQQLSLLMWITQCFLPVFLAQPPSGQERASA TLODLVFDECGITDDOLLALLPSLSLGDPKKLLTQHFVQENYLEYRQVPGSDPACEALEAQQEALGLVCVQAATSSSSPLVLGTLEFYLAMPFATPME AELARRS LAQUA PPLPVEEA PROVRMAAR LOGAAWR LEPEDGTAL CFIFA AEQFS DEVEPAT PEGEPAT OR ODPAAA QEGTMNYPLWSQSYEDSSNO EEEGPSTFPDLESNOEEEGPSTFPDLESEFQAALSRKVAELVHVDLFLKEGACDELFSYLI EKVKRKKNVLRLTIRLTAADHRQLQLSISSCLQQLSL LMWITAAMPLEORSOHCK PEEGLEARGEALGLVGADADGPGGPGI PDGPGGNAGGPGEAGATGGRYEFLWGPRALVETSYVKVLHHMVKI SGGPHITN CRLSEGDVMHLSQSPSVSQLSVLSLSGNYLEYRQVPGSDPACYEFLWGPRALVETSYVIFSKASSSLQLVFGIELMEVDPIGHLYIFQALYVDSLFFL WO 01/090197

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 $\tt RGRLDQLLRHVMNPLETLSYIAQFTSQFLSLQCLQALYVDSLFFLRGRLGQHLHLETFKAVLDGLDVLLAQEVRPRRWKFIRLTAADHRQLQLSISSC$ LQQLSLLMWITCCKKLKIFAMPMQDIKMILKMVQLDSIEDLGAPRGPHGGAASGLNGCCRCGARGPESRLLKKVADLVGFLLLKYRAREPVTKAEMLE SVIYDGLLGDNQIMPKTGFLIIVLVMIAMEGGHSISALQSLLQHLIGLSNLTHVLYPVPLESYIAREGDCAPEEKIWEELSVLEVFEGREDSIDQLLR HVMNPLETLS:ITNCRLSEGDVMHLSRALAETSYVKVLEYVIKVSARVRFFFPSLRSNLTHVLYPVPLESYEDIHGTLHLERLAYLAAMLMAQEALAFL MAQGAMLAAQERRVPRAKNYKHCFPEIFGKASESLQLVFGIDVKEADTLVEVTLGEVPAAESPDPPQSPQGASSLPTHARLRELLCELGRPSMVWLSA NPCPHCGDRVMLTDVSPEPLQALLERASATLQDLVFDECEDEGASAGQGPKPEADSQEQGHPQTGCECEMLGSVVGNWQYFFPVIFSKASSSLQLVF GAAMSWRGRSTYRPRPRRYVEPPEMIGPMRPYISMSVWTSPRRLVELAGQSLLKDEALAIAYDGREHSAYGEPRKLLTQDLVQEKYLEYRQQCFLPVF LAQAPSGQRRAAVKVLHHMVKISGGPHISYPPLHEWVLREGEQLHITMPFSSPMEAELVRRILSRDAAPLPRPGVLLKEFTVSGNILTIRLTAADHRQ LQLSKMILKMVQLDSIEDLEVTCTWKLPTLAKFSFLIIVLVMIAMEGGHAPEEEIWEELSVMEVEVTCTWKLPTLAKFSPYLGQMINLRRLLLSEGLE argealglvgaqapateeqeaassssisypplhewvlregeeaahihassyispekeeqyiaqftsqflslqclgnaggpgeagatggrgprgagaar asgpccgprgagaarasgpcggaprgphggaasglnqgasafpttinftrqrqpsegsssreeegplarrslaqdapplpvpgvllkeftvsgnilaa fdgrhsqtlkamvqawpftclplgvlmkikvsarvrfffpslreaalreeeegvaagitddqllallpslshcsqlttlsfygnsivktpeeemrshy VAQTGILWLLMINCFLINLISSCLQQLSLLMWITQCFLPVFLAQAPSGQYLIEKVKRKKNVLRLCCKKLKIFAMPMQDIAREPVTKAEMLESVIKNYKH CFPEIFGKASLVRRILSRDAAPLPRPGAVLKDFTVSGNLLHCSQLTTLSFYGNSISISALQSLLQHLIGLMVWLSANPCPHCGDRTFYDPEPILCPCF MPAASWSQKRSFVYVWKTWGEGLPSQPIIHTCLLQARLMKEESPVVSWRLEPEDGTALCFIFVYFFLPDHLSFGRPFHLNFCDFLAAPYLGQMINLRR LLLSHIHASSYISPEKEEQQAPATEEQEAASSSSTLVEVTLGEVPAAESQAWPFTCLPLGVLMKGQHLHLETFKAVLDGLSTEAEQPFIPVEVLVDLF LKEGACDELFSAEVPGAQGQQGPRGREEAPRGVRMAARLQGGAPRGPHGGAASAQDGRCPCGARRPDSRLLGPRGAGAARASGPRGGAPRGPHGGAAS AQDLAGQSLLKDEALAIAALELLPRELFPPLFMEPATQRQDPAAAQEGEDEGASAGQGPKPEAPEAAQPMTKKRKVDGLSTEAEQPFIPVEVLGRCPC GARRPDSRLLQLHITMPFSSPMEAEPGAVLKDFTVSGNLLFIRLTAADHRQLQLSEDIHGTLHLERLAYLHARLRELLCELGRPSDSOEOGHPOTGCE CEDGPDGQEMDPPNPEEFVIGLRVWQWEVISCKLIKRATTRQPAADADGPGGPGIPDGPGGNAGGPGEAGATGGRPTGHSYVLVTCLGLSYDGLLGDN QIMPKTGFLLLKYRAREPVTKAEMLGSVVGNWQYFFPTGILWLLMNNCFLNLSPRKPAAEFQAALSRKVAELVHFLLLKYRAREPVTKAVPDSDPARY EFLWGPRALAETSYVKVLEYVGCCRCGARGPESRLLEFYLAMPFATPMEAEATCLGLSYDGLLGDNQIMPKAGLLIIVLAIGNAGGPGEAGATGGRGP RGAGAARASGPRG

#### Artificial DNA:

GCCCCTGAGGAAGAGATTTGGGAAGAGCTCAGCGTCATGGAAGTGTATGACGGAAGGGAACACCTCCGCCTATGGCGAACCCCAGAAAGCTCGAGGAAGT ATAGGGCTAGCCTCTACTCCTTCCCTGAGCCTGAGGCTGCCCAACCCATGACCAAAAAGAGAAAGGTCGACGGACAGATTATGCCTAAGGCTGGCCTC CTGATTATCGTCCTGGCTATCATTGCCAGAGAGGGGAGACTGTGCCCCTGAGGAAAAGATTTGGGAACTGCAAGTGCTCGACCTCAGGAAAAACTCCCA CCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAACTGGATGTGCTCCTGGCTCAGGAAGTGAGACCCAGAAGGT GAGGTCCCCGGAGCCCAAGGCCAACAGGGACCCAGAGGCAGACAGTCCCCCTCCGTGTCCCAGCTCAGCGTCCTGTCCCTGTCCCGGCGTCATGCTCAC CTAGGTATGAGTTTCTGTGGGGCCCTAGGCAACCCTCCGAGGGAAGCTCCAGCAGAGAGGGAAGAGGGAACCCTCCACCTCCTGCATTCTGGAAAGCCTC CGTCGTGTCCACCTTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCTATCGAACTGATGGAGGTCGACCCTATCGGACACC TCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAATAGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGA  ${\tt CCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGAGAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTGT}$ GATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGTGCCGCTATGGAAAGGAGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGT CCGTGTGGACCTCCCCAGAAGGCTCGTGGAAGCCGCTCTGATGGAGACACACCTCAGCTCCAAGAGGATACACAGAGGAAGCCGGAGGCTTTTTCCCT GGGACTGGTCTGCGTCCAGGCTGCCACAAGCTCCAGCTCCCCCCTCGTGCTCGGCACACTGGAAGAGGTCCCCACAGCCGGAAGCACAGACCCTCCCC AAAGCCCTGCCCTCGAGCTCCTGCCTAGGGAACTGTTTTCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAACCCTCAAGGCTATGGTC GAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAAGAGTCCCT GCAACTGGTCTTCGGAATCGATGTGAAAGAGGCTGACCCTACCGGACACTCCTACGTCCTGGTCACCTGTCTGGGACTGTCCCCCGATCCCCCTCAGT GCCCCCAAGGCGCTAGCTCCCTGCCTACCACAATGAATTACCCTCTGTGGAGCCAAAGCTATGAGGATAGCTCCGCCGCTATGCAAGCCGAAGGCCAA GGCACAGGCGGAAGCACAGGCGATGCCGATGGCCCTGGCGGACCGGAATCCCTGACGGACAGGACAGTGTTTCCTCCCCGTCTTCCTCGCCCAACC CCCTAGCGGACAGAGAAGGGCTGCCACCTGGGGCGAAGGCCTCCCCTCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCA GCTTTGGCAGACCCTTTAGCACAAGCTGTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTG AAATACAGAGCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGATGCCGATGCCCTGGCGGACCCGGAATCCCTGACGGACCCGG AGACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGGTCAAGACACCCGAAGAGGGAAATGAGAGAGGCCATTACGTCGCCCAAATCTCCA GCCTCGTGTGTGTGCAAGCCGCTACCTCCAGCTCCAGCCCTTGGGTCCTGGGAACCCTCGAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAG GCTGAGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCTCCCGTCGAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGC TGCCTGGAGACCCGAAGCCGCAACCCGCTCTGTGTTTCATTTTCGCTGCCGAGCAATTCTCCCGACGAAGTGGAACCCGCTACCCCTGAGGAAG GCGAACCCGCTACCCAAAGGCAAGACCCTGCCGCTGCCCAAGAGGGAACCATGAACTATCCCCTCTGGTCCCAGTCCTACGAAGACTCCAGCAATCAG TCTGTCCAGGAAAGTGGCTGAGCTCGTGCATGTGGATCTGTTTCTGAAAGAGGGAGCCTGTGACGAACTGTTTAGCTATCTGATTGAGAAAGTGAAAA CTCATGTGGATCACAGCCGCTATGCCTCTGGAACAGAGAAGCCAACACTGTAAGCCTGAGGAAGGCCTCGAGGCTAGGGGAGAGGCTCTGGGACTGGT  $\tt CGGCGCTGACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGCTACCGGAGGCAGAT$ ACGAATTCCTCTGGGGACCCAGAGCCCTCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCATATCACAAAC TGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTAGCGTCAGCCAACTGTCCGTGGTCAGCCTCAGCGGAAACTATCTGGAATACAG ACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTATGTGATTTTCTCCAAGGCTAGCTCCA AGAGGCAGACTGGATCAGCTCCTGAGACACGTCATGAATCCCCTCGAGACACTGTCCTACATTGCCCCAATTCACAAGCCAATTCCTCAGCCTCCAGTG tctgcaagecetctaegtegaetecetgtttteeetaaggggaaggeteggeeaaeaeeteeaeetegagaeatteaaageegteetggatggeeteg CTCCAGCAACTGTCCCTGCTCATGTGGATCACATGCTGTAAGAAACTGAAAATCTTTGCCATGCCCATGCAGGATATCAAAATGATTCTGAAAATGGT

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TAGCATTAGCGCTCTGCAAAGCCTCCTGCAACACCTCATCGGACTGTCCAACCTCACCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTATATCGCTA GGGAAGGCGATTGCGCTCCCGAAGAGAAAATCTGGGAGGAACTGTCCGTGCTCGAGGTCTTCGAAGGCAGAGAGGATAGCATTGACCAACTGCTCAGG CATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGGAGACGTCATGCATCTGTCCAGGGGCTCTGGCTGAGACAAGCTA CCCTCGAGTCCTACGAAGACATTCACGGAACCCTCCACCTCGAGAGACTGGCTTACCTCGCCGCTATGCCTCATGGCTCAGGAAGCCCTCGCCTTTCTG ATGGCCCAAGGCGCTATGCTCGCCGCTCAGGAAAGGAGAGTGCCTAGGGCTAAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTAGCGA AAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGATACCCTCGTGGAAGTGACACTGGGAGAGGTCCCCGCTGCCGAAAGCCCTGACCCTC AATCCCTGTCCCCATTGCGGAGACAGAGTGATGCTGACAGACGTCAGCCCTGAGCCTCTGCAAGCCCTCCTGGAAAGGGCTAGCGCTACCCTCCAGGA tctggtcttcgatgagtgtgaggatgaggggggcctccggcggacagggacccaaacccgaagccgatagccaagagcaaggccatccccaaaccggat GGAGCCGCTATGTCCTGGAGAGGCAGAAGCACATACAGACCCAGAACCCAGAAGGTATGTGGAACCCCTGAGATGATCGGACCCATGAGGCCTTACAT TAGCATGAGCGTCTGGACAAGCCCTAGGAGACTGGTCGAGCTCGCCGGACAGTCCCTGCTCAAGGATGAGGCTCTGGCTATCGCTTACGATGGCAGAG AGCATAGCGCTTACGGAGAGCCTAGGAAACTGCTCACCCAAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAACAGTGTTTCCTCCCCGTCTTC ATGCCGCTCCCCCAGACCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAA CTCCTTCCTCATCATTGTGCTCGTGATGATCGCTATGGAAGGCGGACACGCTCCCGAAGAGGGAAATCTGGGAGGAACTGTCCGTGATGGAGGTCGAGG TCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCCGAGGGACTGGAA CGAATGGGTCCTGAGAGAGGGGAGGGAAGCCGCTCACATTCACGCTAGCTCCTACATTAGCCCTGAGAAAGAGGAACAGTATATCGCTCAGTTTACCT CCCAGTTTCTGTCCCTGCAATGCCTCGGCAATGCCGGGGGCCCTGGCGAAGCCGGAGGCCACAGGGGGGACCCAGAGGCGCTGGCGCTGCCAGA GCCTCCGGCCCTGGCGGAGGCCCTAGGGGAGCCGGAGCCGCTAGGGGTAGCGGACCCGGAGGCGGAGCCCCTAGGGGACCCCCATGGCGGAGCCGCTAG CTCTGGCTAGGAGAAGCCTCGCCCAAGACGCTCCCCCTCTGCCTGTGCCTGGCGTCCTGAAGGAATTCACAGTGTCCGGCAATATCCTCGCCGCT TTCGATGGCAGACACTCCCAGACACTGAAAGCCATGGTGCAAGCCTGGCCCTTTACCTGTCTGCCTCTGGGAGTGCTCATGAAAATCAAAGTGTCCGC TCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACACTGTCCTTCTATGGCAATAGCATTGTGAAAACCCCTGAGGAAGAGATGAGGTCCCACTAT GTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTCATCTCCAGCTGTCTGCAACAGCTCAGCCTCCTGATGTGGATTAC AAAAGCTCAAGATTTTCGCTATGCCTATGCAAGACATTGCCAGAGAGCCTGTGACAAAAGGCTGAGATGCTGGAAAAGCGTCATCAAAAACTATAAGCAT TGCTTTCCCGAAATCTTTGGCAAAGCCTCCCTGGTCAGGAGAATCCTCAGCAGAGACGCTGCCCTCTGCCTAGGCCTGGCGCTGTGCTCAAGGATTT CACAGTGTCCGGCAATCTGCTCCACTGTAGCCAACTGACAACCCTCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCTCCAGTCCCTGCTCCAGC ATCTGATTGGCCTCATGGTCTGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTT ATGCCTGCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGAGAGGGACTGCCTAGCCAACCCATTATCCATACCTGTCT GCTCCAGGCTAGGCTCATGAAAGAGGAAAGCCCTGTGGTCAGCTGGAGGGTCGAGGCCTGAGGATGGCACAGCCCTCTGCTTTATCTTTTGTGTATTTCT TTCTGCCTGACCATCTGTCCTTCGGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCCCCCTATCTGGGACAGATGATCAATCTGAGAAGG CTCCTGCTCAGCCATATCCATGCCTCCAGCTATATCTCCCCCGAAAAGGAAGAGCAACAGGCTCCCGCTACCGAAGAGCAAGAGGCTGCCTCCAGCTC AGCATCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGACTGTCCACCGAAGCCGAACAGCCTTTCATTCCCGTCGAGGTCCTGGTCGACCTCTTC CTCAAGGAAGGCGCTTGCGATGAGCTCTTCTCCGCCGAAGTGCCTTGGCGCTCAGGGACAGGCCCTAGGGGAAGAGGGAAGAGGCTCCCAGAGGCGT GGAGCCTGCCACACAGAGACAGGATCCCGCTGCCGCTCAGGAAGGCGAAGACGAAGGCGCTAGCGCTGGCCAAGGCCCTAAGCCTGAGGCTCCCGAAG CCGCTCAGCCTATGACAAAGAAAAGGAAAGTGGATGGCCTCAGCACAGAGGCTGAGCAAACCCTTTATCCCTGTGGAAGTGCTCGGCAGATGCCCTTTGC GGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTCTCCAGCCCTATGGAAGCCGAACCCGGAGCCGTCCTGAAAGACTT TACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCCGAGGATATCCATGGCACACTGCATCTGGAAA GGCTCGCCTATCTGCATGCCAGACTGAGAGAGCTCCTGTGTGAGCTCGGCAGACCCCTCCGACTCCCAGGAACAGGGACACCCCTCAGACAGGCTGTGAG TGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAATTCGTCATCGGACTGAGAGTGTGGCAGTGGGAGGTCATCTCCTGCAA ACTGATTAAGAGAGCCACAACCAGACAGCCTGCCGCTGACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGAC CCGGAGAGGCTGGCGCTACCGGAGGCAGACCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAAC CAAATCATGCCCAAAACCGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGGCTCGGCTCGGCAATTGGCA ATACTTTTTCCCTACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCTGAGTTTCAGGCTGCCCTCA GCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGCCAGAGAGCCTGTGACAAAGGCTGTGCCTGACTCCGACCCTGCCAGATAC GAATTCCTCTGGGGACCCAGAGCCCTCGCCGAAACCTCCTACGTCAAGGTCCTGGAATACGTCGGCTGTTGCAGATGCGGAGCCAGAGGCCCTGAGTC CAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAAGCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATA ACCAAATCATGCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATTGGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGGACCC AGAGGCGCTGGCGCTGCCAGAGCCTCCGGCCCTAGGGGA



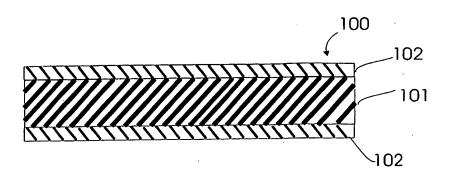


FIGURE 28

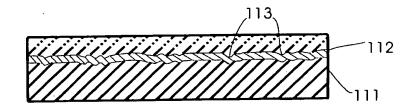


FIGURE 29

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#### Cassettes for construction of a full-length HIV Savine

#### Cassette Al

ggatccaccATGACAGGCCCTTGCACAAACGTCAGCACCGTGCAATGCACACACGGAATCAGACCCGTCGTGTCCA CCCAACTGCTCCTGAATGGCTCCCTGAGAAGCCTCTACAATACCGTCGCCACACTGTGGTGCGTCCACCAAAGGAT TGACGTCAGGGACACAAAGGAAGCCCTCGACAAAATCGAACTCGGCGATGGCGGAGGCGCTGAAAGGCAAGGCACC CCGATATGGTGATTTACCAGTACATGGACGATCTGTATGTGGGAAGCGATCTGGAAATCGGACAGCATTTTACCAC ACCCGATAGAAACACCAAAAGGAACCACCATTCCTCTGGATGGGATACGAACTGCATCCCGATAGGTGGACCGTC CAGCCTCTTAATTTCCCTCAGATTACCCTCTGGCAGCGTCCCCTCGTGACAATCAAAATCGGCGGACAGCTCATAG AGGCTCTGCTCGACACGGCTCCTATGGCAGAAAGAAACGTAGGCAACGTAGACGCGCTCCTCAGAGCAGCAAGGA TCACCAATACCCTATCTCTGAGCAACCCCTCTCCTTCTTTAGGGAAAACCTGGCTTTCCAGCAAGGTAAAGCCAGA GAGTTTTCCAGCGAACAGACAAGAGCCAATAGCTCCGCCTCCAGGAAGAGCCCCCAAATCTCCGGCGAAAGCTCCG TCATTCTGGGATCTGGCACCAAAAACGCCGCTACTAGAAGAATCGAAGTGAAAGATACCAAAGAGGCTTTGGATAA GATTGAGGAGGTGCAAAAGAAAAGCGAGCAAAAGACACAACAGGCTGCCGCTAAAGCCGGATACGTCACCGATAGG GGAAGGCAAAAGATTATCTCCCTGACAGAGACAACCAATCAGAAAAACCGAACTGCATGCCATTCAAGAAGCCACTA  ${\tt CCACACTGTTTTGCGCCAGCGATGCCAAAGCCTATGAGACAGAGGTCCACAATGTGTGGGCCACACACGCTTGCGT}$ CCCCGCTGACGATACAGTGCTGGAGGAGATGAACCTCCCCGGAAAATGGAAGCCTAAGATGATTGGCGGAATCGGC GGATTCATTAAGGTGAGAAAAATCGGACCCGAAAACCCTTACAATACCCCAATCTTCGCTATCAAGAAAAAGGACT CCACCAAATGGAGAAAGCTCGTGGATTTCAGAGTTAGGATTATCAATATCCTCTACCAAAGCAATCCCTATCCTAG AGACTGGTCAACGGATTCTTAGCCCTCGCCTGGGACGATCTGAGAAACCTCTGCCTCTTCGAAAACCTCTGGGTCA CCGTCTACTATGGCGTCCCCGTCTGGAGAGAGGCTGCCACAACCCTCTTCTGTGCCTCCGACGCTAAGGCTTACGC TGCCATGGCTGGCAGAAGCGGCGCACAGACGAAGAGCTCCTGAGGGCTATCAGAATCATTAACATTCTGTATCAG TCCAACCCTTACCCTTCCGCTAGTATGAGAATCAGAACCTGGAACAGCCTGGTCAAGCATCACATGCACATCTCCA AGAAAGCCAAAGGCTGGTTCTATAGGCATCACTTTGAGGAGTCCGAGCTCGTGAATCAGATTATCGAAAAGCTCAT CAAAAAGGAAAAGGTCTACCTATCATGGGTACCAGCCCACAAGGGAATCGGACAAACCAAAGAGCTCCAGAAACAG ATTATCAAAATCCAAAACTTTAGGGTCTACTATAGGGATAGCAGAGACCCTATCTGGAAGGGACCCAAAAGCTTTG TCTGAAACCCGAACCCACAGCCCCTCCCGCTGAGAATTTCAGATTCGGTGAGGAAACTACACCCTCCCAAAAGCAA GAGCAAAAGGATAAGGAGCAATACGATCAGATTCTTATTGAGATTTGCGGCAAGAAAGCTATTGGTACGGTGCTCG TGGGACCTACCCCTGTGAATATCATTGGCAGAATTTACGAAACCTATGGCGATACCTGGGAGGGCGTCGAGGCTCT GATCAGAATCCTCCAGCAACTGATGTTTATCCATTTCAGAATCGGATGTTTTCATTGCCAAGTGTTTTTCTCACC TGGACCCCAAGCTGGAGCCTTGGAAACACCCTGGCTCCCAGCCTAAGACAGCCTGTTACAAATGCTATTGCAAAAA CTCAAGTCCCTGTTTGGCAATGACAATTTCAATATGTGGAAGAATGACATGGTGGAACAGATGCAAGAAGACATTA TCTTACTATGGGACCAAGCCTCAAGCCTTGCGTCAAGCTCGACGTCGCGATGCCTATTTCTCCGTGCCTCTGGA GGCCAAGTGAATTGCTCACCAGGCATTTGGCAACTGGATTGCACACCCTGGAGGGAAAGATTATCCCTAAGGTCA TAGCATGGATGACCTCTACGTCGGCTCCGACCTGG



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AGATTGGCCAACATAGGACCAAAATCGAAGAGCTCAGGGAACACCTCCTGAAATGGGGACTCACCGAAACCACAAA CAGACAATGGCAGGACAAAGATTGAGGAACTGAGACCGCATCTGCTCAAATGGGGCTTCACAACCCCTGACAAAAA AGAGACGCAGAGAAAATCACACAATGAATGGCCATACTGCCACAGAGTCCCAGAATCAGCAAGACAGAAACGAAA AGGAACTGCTGGAGCTCGACAAATGGGCAAGCCTCTGGAATTGGTTTAACATTACCGACACCGGAAATAGCTCCAA AGTGTCCCAGAATTACCCTATCGTCCAGAATGTCCAAGGCCAAATGGTCCACCAACCCCTCTCCCCCAGACTCATC GGACTGAGAATCGTTTTCGCTGTGCTCAGCATTATCAATAGGGTCAGGCAAGGCTATAGCCCTCTGTCCTTCCAAA CCCTCCCCTCATCCATCTGCAATACTTTGACTGTTTCGCTGACTCCACCATTAGGAGAGCCATCTTGGGACACAT AGTGAGAAGGAGATGCGAATACGCTGTGGGACTCGGAGCCATGTTCCTTGGCTTCTGGGTGCCGCTGGCTCCACC ATGGGCGCTGCCTCCATGACACTGACAGTGCAAGCCTATGACCCTAGCAAAGACCTCATTGCTGAGATTCAGAAAC  $\tt CGTCAACATCATCGGAAGGAACATGCTGACACAGCTTGGCCGCACTCTCAACTTTCCCATTAGCAAAGGCAGCCCT$ GCTATCTTTCAGTCCAGCATGCCACAGATTCTGGAGCCTTTTAGGATAAAAAACCCTGAGATGGTCATCTATCAGT ATCCTAGCCCTCTGACATTCGGATGGTGTTTCAAACTGGTCCCCGTGGACCCCAGCGAAGTGGAAGAGATCAACAA GGGCGAAAACAATTGCCCCCTGTTTAGGAAATACACAGCCTTTACCATTCCCTCCATCAATAACGAAACCCCTGGC ATTAGGTATCAGTATAACGTCCTGCCTCAGGGATGGGGAAGCACAATGGGAGCCGCCAGCATGACCCTCACCGTCC AGGCTAGGCTACTGCTCAGCGGAATCGTCCAGCAACAGAGCAATCTGCTGGAGGAGAATAGGGAAATCCTCAGAGA GCCTGTGCATGGCGTCTACTACGATCCCTCCAAGGATCTGGTCGCTGAAATCCAAAAGCAAGGCAGAGAAACTG TCCACCATGGTGGATATGGGAAACTACGACCTCGGAGTGGACAATAACCTCGCCGCTATTAGAATCCTGCAACAGC TCATGTTCATTCACTTTAGGATTGGCTGCCAGCACTCCAGGATTGGCATCATCCGTCAGAGAAGGGCCAGAGCTCC CAGGAAAAAGGGATGCTGGAAGTGTGGCAGAGAGGGACACCAGATGAAGGATTGCACTGAGAGACAGGCTAACTTT ATGGCGTCAGCATTGAGTGGAGGATAAGGGAAAGGGCTGAGGATAGCGGCAACGAAAGCGAAGGCGACACAGAAAGA GCTCAGCACATTGGTGGACATGGGCAATTACGATCTGTCTAGCCCTGCCCCCAGGGGACCCGATAGGCTGGAGAGA ATCGAAGAGGAAGGCGAGAGCAAGGCAGAGGCAGAAGCGTCAGGCTCGTGAATGGCAGAGAGGTCGAGGAAGTCA GTGGCCAGCTTCTCTCCGAGCAAACAGGGGCTAACTCCTCTACAAGCAGAAAGCTGGGAGACGGAGGCGGAGCCG ACAGACAGGGAACAAGCTCCAGCTGTTTCAATTGCGGCAAAGAGGGGACACATTGCCAAAAACTGTAGGGCCCCTCG CAAGAAAGGTTGTTGGAAATGCGGAAAGGAAGGCCATCAAATGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTC GGCAAAATCTGGCCCTCCAACAAAGGCAGACCGGGAAACTTTCTCCAAAGCAAATGGCTCTGGTATATCAAAATCT TTATCATGATCGTCGGTGGACTGATTGGCCTCAGGATTATCTTTGCCGTCCTGTCCATCGTTAACGGAGCCGTGAG CCGAGACCTCGATAAACATGGCGCTATTACAAGCTCCAATACCGCTGCCAATAACGCTGACTGTCTGGCTGAAG GCTGCTGCCATGACACCCCTGGAGATCATCGCTATCGTCGCCTTTATCGTCGCCCTCATCATAGCCATTGTGGTCT GGACAATCGTCTACATTGAGTATGTCGACtgaagatctgaattc

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#### A2 fragment

ggatccaccATGACAGGCCCTTGCACAAACGTCAGCTCCGTGCAATGCACACAGGAATCAAACCCGTCGTGTCCA CCCAACTGCTCCTGAATGGCTCCCTGAAAAGCCTCTACAATACCGTCGCCACACTGTGGTGTGTCCACCAAAGGAT TGAGGTCAAGGACACAAAGGAAGCCCTCGACAAAATCGAACTCGGCGATGGCGGAGGCGCTGAAAGGCAAGGCACC TCCAGCTCCATCAACTTTCCACAAATCACACTGTGGCAAAGGCCTCTGGTCACCGAACCCTTCAGAAAAGAGAATC CCGAAATGGTGATTTACCAGTACATGGACGATCTGTATGTGGGAAGCGATCTGGAAATCGGACAGCATTTTACCAC ACCCGATAAGAAACACCAAAAGGAACCACCATTCCTCTGGATGGGATACGAACTGCATCCCGATAGGTGGACCGTC CAGCCTTTTAATTTCCCTCAGATTACCCTCTGGCAGCGTCCCCTCGTGACAATCAAAATCGGCGGACAGCTCATAG AGGCTCTGCTCGACACAGGCTCCTATGGCAGAAAGAAACGTAGGCAACGTAGACGCCTCCTCAGAGCAGAAAGGA TCACCAATACCCTATCTCTGAGCAACCCCTCTCCTTCTTTAGGGAAAACCTGGCTTTCCAGCAAGGTAAAGCCAGA GAGTTTTCCAGCGAACAGACAGGAGCCAATAGCTCCGCCTCCAGGAAGAGCCCCCAAATCTCCGGCGAAAGCTCCG TCATTCTGGGATCTGGCACCAAAAACGCCGCTACTAGAAGAATCGATGTGAGAGATACCAAAGAGGCTCTGGATAA GATTGAGGAGGAGCAAAACAAAAGCAAGCAAAAGACACAACAGGCTGCCGCTAAAGCCGGATACGTCACCGATAGG GGAAGGCAAAAGATTATCTCCCTGACAGAGACAACCAATCAGAAAACCGAACTGCATGCCATTCAAGAAGCCGATA  ${\tt CCACACTGTTTTGCGCCAGCGATGCCAAAGCCTATGACACAGAGGTCCACAATGTGTGGGCCACACACGCTTGCGT}$ CCCCGCTGACGATACAGTGCTGGAGGAGATGAACCTCCCCGGAAAATGGAAGCCTAAGATGATTGGCGGAATCGGC GGATTCATTAAGGTGAGAAAGATCGGACCCGAAAACCCTTACAATACCCCAATCTTCGCTATCAAGAAAAAGAACT CCACCAAATGGAGAAAGCTCGTGGATTTCAGAATTAGGATTATCAAAATCCTCTACCAAAGCAATCCCTATCCTAG CTCCGAAGGCACCAGGCAAACCAGAAAGAATAGGAGAAGGGGATGGGGAGGCGAACAGGGTAGGGATAGGTCCGTG AGACTGGTCAACGGATTCTTAGCCCTCGCCTGGGACGATCTGAGAAGCCTCTGCCTCTTCGACAACCTCTGGGTCA CCGTCTACTATGGCGTCCCCGTCTGGAGAGAGGCTAACACCCTCTTCTGTGCCTCCGACGCTAAGGCTTACGC TGCCATGGCTGGCAGCAGCAGCACCAGACGAAGAGCTCCTGAAGGCTGTCAGAATCATTAAGATTCTGTATCAG TCCAACCCTTACCCTTCCGCTAGTATGAAAATCAGAACCTGGAAGAGCCTGGTCAAGCATCACATGTACATCTCCA AGAAAGCCAATGGCTGGTTCTATAGGCATCACTTTGAGGAGTCCGAGGTCGTGAATCAGATTATCGAAAAGCTTAT CAAAAAGGAAAAGGTCTACCTATCATGGGTACCAGCCCACAAGGGAATCGGACGAACCAAAGAGCTCCAGAAACAG ATTATCAAAATCCAAAACTTTAGGGTCTACTATAGGGATAGCAGAGACCCTATCTGGAAGGGACCCAAAAGCCTTG TCTGAGACCCGAACCCACAGCCCCTCCCGCTGAGAATTTCGGATTCGGTGAGGAAACTACACCCTCCCAAAAGCAA GAGCCAAAGGATAAGGAGCAATACGATCAGATTATTATTGAGATTTGCGGCAAGAAAGCTATTGGTACAGTGCTCG TGGGACCTACCCCTGTGAATATCATTGGCAGAATTTACGAAACCTATGGCGATACCTGGGAGGGCGTCGAGGCTCT GATCAGAATCCTCCAGCAACTGATGTTTATCCATTTCAGAATCGGATGTTTTCATTGCCAAGTGTGTTTTCTCACC TGGACCCCAACCTGGAGCCTTGGAAACACCCTGGCTCCCAGCCTAAGACAGCCTGTAACAAATGCTATTGCAAAAA CTCAAGTCCCTGTTTGGCAATGACAATTTCAATATGTGGAAGAATAACATGGTGGAACAGATGCAAGAAGAACATTA TCTCACTATGGGACCAAAGCCTCAAGCCTTGCGTCAAGCTCGACGTCGGCGATGCCTATTTCTCCGTGCCTCTGGA GGCCAAGTGAATTGCTCACCAGGCATTTGGCAACTGGATTGCACACCTGGAGGGAAAGATTATCCCTAAGGTCA TAGCATGGATGACCTCTACGTCGGCTCCGACCTGGAGATTGGCCAACATAGGACCAAAATCGAAGAGCTCAGGGCA



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CACCTCCTGAGATGGGGACTCACCGACACCACAAACCAAAAGACTGAGCTCCACGCTATCCATCTGGCTCTGCAAG ACTCCGGCTTAGAGGTCAACATTGTGACAGACATTCCCGCTGAGACTGGTCAAGAGACCACCTATTTCATTCTGAA ACTGGCTGGCAGATGGCCTGTGAGAATCATTCACACAGACAATGGCAGGACAAAGATTGAGGAACTGAGACCGCAT CACAGAGTCCCAGAATCAGCAAGACAGAAACGAAAAGGAACTGCTGGAGCTCGACAAATGGGCAAGCCTCTGGAAT TGGTTTAACATTACCGACACCGGAAGTAGCTCCCAAGTGTCCCAGAATTACCCTATCGTCCAGAATCTCCAAGGCC AAATGGTCCACCAACCCATCTCCCCCAGACTCGTCGGACTGAGAATCATTTTCGCTGTGCTCAGCATTATCAATAG GACTCCACCATTAGGAGAGCCATCCTTGGACACAGAGTGAGCAGGAGATGCGAATACGCTGTGGGAATCGGAGCCA TGTTCCTTGGCTTTCTGGGTGCCGCTGGCTCCACCATGGGCGCTGCCTCCATCACACTGACAGTGCAAGCCTATGA CCCTAGCAAAGACCTCATTGCTGAGATTCAGAAACAGGGTCAGGATCAGTGGACATATCAGATTTTCCAAGAGCCT GCACCCTCAACTTTCCCATTAGCAAAGGCAGCCCTGCTATCTTTCAGTCCAGCATGACACAGATTCTGGAGCCTTT TAGGAAACAAAACCCTGACATGGTCATCTATCAGTATCCTAGCCCTCTGACATTCGGATGGTGTTTCAAACTGGTC CCCGTGGACCCCAGCGAAGTGGAAGAGACCAACAAGGGCGAAAACAATTGCCTCCTGTTTAGGAAATACACAGCCT TTACCATTCCCTCCACCAATAACGAAACCCCTGGCATTAGGTATCAGTATAACGTCCTGCCTCAGGGATGGGGAAG CACAATGGGAGCCGCCAGCATGACCCTCACCGTCCAGGCTAGGCAACTGCTCCAGCGGAATCGTCCAGCAACAGAAC AATCTGCTGGAGGAGAATAGGGAAATCCTCAAAGAGCCTGTGCATGGCGTCTACTACGATCCCTCCAAGGATCTGA TCGCTGAAATCCAAAAGCAAGGCACAGAGGAACTGTCCGCCTTGGTGGATATGGGAAACTACCACCTCGGAGTGGA ATTGGCATCATCCGTCAGAGAAGGGCCAGAGCTCCCAGGAAAAAGGGATGCTGGAAGTGTGGCAAAGAGGGACACC AGATGAAGGATTGCACTGAGAGACAGGCTAACTTTCTGGGAAAGGATGCCAGACTGGTTATCAAAACCTATTGGGG ACTGCATACCGGTGAGAGAGACTGGCACCTCGGCCATGGCGTCAGCATTGAGTGGAGGACAAGGGAAAGGGCTGAG GATAGCGGCAACGAAGCGAAGGCGACAGAGAGAGAGCTCAGCACAATGGTGGACATGGGCAATTACGATCTGTCTA GCCCTGCCCCAGGGGACCCGATAGGCTGGAGAGAATCGAAGAGGAGGCGAGAGCAAGACAGAAGACAGAAGCGT CAGGCTCGTGAATGGCAGTGAGGGCGAGGAAGTCAATAAGGGAGAGAATAACTGTCTGCTCCACCCTATGAGTCAA CATGGCATGGAAGACGAAGACAGAGAGGGTCAATAGCGATATCAAAGTGGTCCCCAGAAGGAAAGCCAAAATCATTA GAGGGACACATTGCCAAAAGCTGTAGGGCCCCTCGCAAGAAAGGTTGTTGGAAATGCGGAAGGGAAGGCCATCAAA TGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTCGGCAAAATCTGGCCCTCCAAAAAAAGGCAGACCCGGAAACTT TCTCCAAAGCAAATGGCTCTGGTATATCAAAATCTTTATCATGATCGTCGGTGGACTGATTGGCCTCAGGATTATC TTTGCCGTCCTGTCCATCATTAACGGGGCCGTGAGCCGAGACCTCGATAAACATGGCGCTATTACAAGCTCCAATA CCGCTGCCAATAACCCTGACTGTGTCTGGCTGGAGGCTGCTGCCATGACACCCCTGGAGATCATCGCTATCGTCGC CCTTATCGTCGCCCTCATCATAGCCATTGTGGTCTGGACAATCGTCTACATTGAGTATGTCGACtqaaqatctqaa ttc

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#### B1 fragment

ggatccaccATGCTCGAGAATATGCTCACCCAAATCGGATGCACACTGAATTTCCCTATCTCCCCCATTGAGACAG TGCCTGTGAAACTGAAACCCGGAATGGATGGCGCCGCCACCTTTAGGCCTGGCGGAGGCAATATCAAAGACAATTG GAGAAGCGAACTGTATAAGTATAAGGTCGTGAAGATTAAGCCTCTGGGAATCACATGGATTCCCGAATGGGAGTTC GTCAACACCCCCACTGGTCAAGCTATGGTATCAGCTGGAGAAAGACCCTATCGTTGGCGTTGAGCCTCAGGATC CTCTGTCCTGTTTCTGGATGGCATTGACAAAGCTCAAGAGGAACATGAAAAGTATCACTCCAACTGGAGGACAATG GCCAACGACTTTAATCTGATGAAGCATCTCGTCTGGGCCTCTAGGGAGCTGGAGAGATTCGCTCTGAATCCCAGCC TGTCAAAACCATTATCGTCCAACTCAACGAAAGCGTCGAGATTAACATGGGCGCTAGGGCTAGTGTCCTCAGAGGC GGCAAGCTGGAĊGCCTGGGAAAAGATTAGGCTCAGGCCTGGCGGAAAGAAAAAGTATAGGCTCAAGGAGAAGGAG GCCTGGAGGGACTGGTTTACTCCAAAAAGAGGCAAGACATTCTGGATCTGTGGGTGTATAACACACAGGGATTCAC TAGATGGGGAACCATGATCCTCGGCTTGGTGATTATCTGTAGCGCCAGCGAGAATCTGTGGGTGACAGTGTATTAC GGAGTGCCTGTGTGGAGGAGACAGCTCCTGTCCGGCATTGTGCAACAACAAAATAACCTCCTGAGGGCTATCGAAG CCCAACAGCATCTGCTCCAGCTCACCGTCTGGGTCAGGCATTTCCCCCAGGCCTTGGCTCCACGGCCTGGGACAGTA CATCTATGAGACATACGGAGACACATGGGCGGGAGTGGAAGCCCTCACAGCCCTCATCACACCCAAAAAGATTAGG CCTCCCTCCCATCCGTGAAAAAGCTCACCGAAGACAGATGGAATGAGCCTCAAAAGACATATAGCGCTGGCGAAA GGATTATCGATATCATTGCATCCGACATTCAGACTAAGGAACTGCAAAAGCAAATCCTAAAGATTCAGAATTCGC GCCACCGATATCATTCCCGTGGGCGAAATCTATAAGAGATGGATCATTCTGGGACTCAACAAAATCGTGAGAATGT ATCTACCCGTCAGCATTCTGGATATCAGAGTGAGACAGGGATACTCCCCCCTCAGCTTTCAGACACTGCTGCCCGC CCTCTGCCTCAGACAAGGGGAGACAATCCCACAGACCCTAAGGAAAAGCAAAAAAGGCTAGTGGAGGGGTCGAGTCCA TGAATAAGGAACTGAAAAAGATTATCGGACAGGTCAGGGACCAGGCTGAGCACCTGAAAAACCGCTGTGCAAATGGC TGCCATGCAGATGCTCAAGGATACCATTAACGAAGAGGCTGCCGAGTGGGACAGAGTCCATCCCGTCCATGCCGGG CCCGTTCCCCCTCTCACCGAGATTTGTAAAGAAATGGAAAAAGAAGGCAAAATCTCCAAGATTGGCCCTGAGAATC CCTATAACACCCCATCTTTGCCATTCAAGTGAGAGAGCCAAGCCGAACACCTCAAGACAGCCGTCCAGATGGCAGT GACTTTAGGGAGCTCAACAAACGTACACAGGATTTCTGGGAGGTCCAGCTCGGCTTTTTGGCTCTGGCTTGGGATG ACCTCAGGAGCCTGTGTCTGTTCAGCTATCACAGACTGAGAGACTTTATCCTCATCGTTGCCAGAATCTGCCGACA GACCCCATTCCCATTCACTATTGCGCTCCCGCTGGCTTCGCTATCCTCAAGTGTAACGATAAGAACTTCAATGGCG AAGAGGATTGGCATCTGGGACAGGGAGTGTCCATCGAATGGAGACAGAAAAGCTATAGCACACAGGTGGACCCTGA  $\tt CCTCGCCGATCAGCCTAGCCTCTCTCCCTTAGCTTCCCTGAAAAGCCTCTTCGGAAACGATCCCTTATCCCAA$ GCCGCTAGAAGGGCTATCCTCGGCCATATAGTCAGGAGAAGGTGTGAGTATCAGTCCGGACACAATAAGGTCGGCT CCCTGCAATACCTCGCACTCAGTCAACCCACAACCGCTTGCTACAAGTGTTACTGTAAGAAATGTTGCTTCCACTG AGCAGGCAAGACGAAGACGCAGCCAAGTACCATAGCAATTGGAGAACCATTGGCAATGAGTTTAACCTCCCCCCTA TCGTCCCTAAGGAAATCGTCGCAAATTGCAATAAGTGTAACGAATGGACACTGGAACTGCTGGAGGAACTGAAACA TGAAGCCGTGAGACACTTTCCCAGACCCTGGCTGCATGGCCTCGGTCAACACGATATCATTAGCCTCTGGGATCAG



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TCCCTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTGATGAAGAGAT ACTCCACCCAAGTGGACCCGATCTGGCTGACCAACTGATTCACCTCCACTATTTCGATTGCTTTGCCGATAGCGC AATCCATCCCATCGGCCAACACGGAATGGAGGATGAGGATAGGGAAGTGCTGAAATGGAAATTCGATAGCCATCTG TGAAACACTGGCCCCTCACCGAAGAGAAAATCAAAGCCATTTGGCCTAGCAACAAGGGAAGGCCTGGCAATTTCCC GCAGTCCAGGCCTGAGCCTACCGCACCCCAGCCGAGAGCTTTAGATTCGGCATTAGCAAAAAGGCTAAGGGATGG TTTTACAGACACCATTACGATAGCCGACACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCGGCATGATGACCG CTTGCCAAGGCGTCGGCGGACCCAGTCACAAAGCCAGGGTACTGGCAGAGGCTATATCCCAGGTGAACAACGCTAA CATTCCTCCCATTGTGGCCAAAGAGATTGTGGCAAACTGTGACAAATGCCAGCTCAAGAGTGAGGCTATTCACGGA CAGGTGAACTGTAGCCCTTCCGAGGGAACAAGACAGACTAGGAAGAACAGACGTAGAAGGTGGCGTGCGAGGCAAA GGCAAATCCACTCCATCTCCGAGAGGATTCTGGGACAGATGAGGGAACCCAGAGGCTCCGACATTGCCGGTACTAC AAGCACACTGCAAGAGCAAATCGCATGGATGACAAGCAATCCCCCTAGCATTCAACAAGAGTTTGGCATTCCCTAT AACCTTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTAAAGAAATCATTGGCAGACAGGAGATCCTCG ATCTCTGGGTCTACCATACCCAAGGCTATTTCCCTGACTGGCAGAATTACACCCCGGACCCGGAGTCAGATACCC TAGCAGAGAAAGACAGAGACAGATTCATTCTATTAACGAATGGATTCTCAGCAACTGCCTCGGCAGATCCGCTGAG CCTGTGCCTCTGCAACTGTATAAGACACTGAGAGCCGAACAGGCTACCCAAGAGGTCAAGAATTGGATGACCGAGA CACTGCTCGTGCAAAACGCTAACCCTGACTGTGAGAGAGTGTATCTGGCTTGGGTCCCCGCTCATAAAGGCATTGG CGGAAACGAACAGGTGGACAAACTGGTCAGCGCTGGCATTAGGAAAACAGACCCTAACCCTCAGGAAATCCATCTG TGAAATGCAATAACAAAAGGTTCAACGGAACTGGACCCAGTAAGAATGTGTCCACCGTCCAGTGTACCCATGGCCT AGAGCTCAAGAATAGCGCTATCTCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGGACCGATAGGGTTATC GAAGTGGTTCAGTCCCGGCATCCCAAAGTGTCCAGCGAAGTGCATATCCCTCTGGGAGACGCTAGGCTCATCATTA GGACATACTGGGGCCTCCACACAGGCGCTGCTATGGGCGGTAAATGGTCCAAGTGCTCCCTCGTCGGATGGCCCGC AGTGAGAGAGAGAATCAGACAGACACCCCCTGCCGCTGAGGGGAGTGCTCAAGACCGGCAAGTACTCTAGGAAGAGG GGTGCCCATACCAATGACGTCAAGCAACTGACAGAGGCTGTGCAAAAGATTGCCACAGAGTCTAGCTGGGAGGGTC TGAAATACTGGGGGAATCTGCTCCAGTACTGGGGCCAGGAACTGAAAATCTCCGCCGTCAGCCTCCTGAATGCCAC AGCCATTGAGCTGCCTGAGAAAGAAAGCTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCA TCCCAGATTTACCCCGGAAGAGCCATTGAGGCTCAGCAACACATGCTGCAACTGACAGTGTGGGGCATTAAGCAAC TGCAAGCCAGAGTGCTCGCCATTGAGAGATACCTCGCCCTCCAGGATAGCGGATTGGAAGTGAATATCGTCACCGA TAGCCAATACGCTCTAGGCATCATTCAGGCTCAGCCTGACAAAAGCGAAAAGGGAAATCTCCAACTATACCAATCAG ATTTACAAGATCCTCACCGAATCTCAAAATCAACAGGATAGGAATGAGAAAGACCTCCTGGCTCCCACAAAGGCTA AGAGAAGGGTCGTGCAAAGGGAAAAGCGTGCCGTCGGCATTGGCGCTATGTTTCTCGGATTCCTCGGCGCTCCAA ACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGACCAAATCCTTATCGAAATCTGTGGA AACAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGTCGCTAGGATTGTGGAACTGCTCGGCCGTA GCTCCCTGAAAGGCCTCCAGAGAGGCACACTGAATGCCTGGGTGAAAGTGATTGAGGAAAAGGGATTCAGTCCCGA AGTGATTCCCATGTTTTCCGCTCTGTCCGAGGGAGCCACACTCGAGtgaagatctgaattc

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#### B2 fragment

qqatccaccATGCTCGAGAATATGCTCACCCAAATCGGATGCACACTGAATTTCCCTATCTCCCCCATTGACACAG TGCCTGTGAAACTGAAACCCGGAATGGATGGCGCCGCCATCTTTAGGCCTGGCGGAGGCAATATGAAAGACAATTG GAGAAGCGAACTGTATAAGTATAAGGTCGTGAAGATTAAGCCTCTGGGAATCACATGGATTCCCGAATGGGAGTTC GTCAACACCCCCCACTGGTCAAGCTATGGTATCAGCTGGAGAAAGAGCCTATCGTTGGCGCTGAGCCTCAGGATC CGCTGTCCTGTTTCTGGATGGCATTAACAÄAGCTCAAGAGGAACATGAGAAGTATCACTCCAACTGGAGGACAATG GCCAACGACTTTAATCTGATGAAGCATCTCGTCTGGGCCTCTAGGGAGCTGGAGAGATTCGCTCTGAATCCCGGCC TGTCAAAACCATTATCGTCCACCTCAACGAAAGCGTCGAGATTAACATGGGCGCTAGGGCAAGTGTCCTCAGCGGC GGCAAGCTGGACGCCTGGGAAAAGATTAGGCTCAGGCCTGGCGCAAGAAAAAGTATAGGCTCAAGGAGAAGGGAG GCCTGGACGGACTGATTTACTCCCAAAAGAGGCAAGACATTCTGGATCTGTGGGTGTATAACACACAGGGATTCAC TAGATGGGGAACCTTGATCCTCGGCTTGGTGATTATCTGTAGCGCCAGCGAGAATCTGTGGGTGACAGTGTATTAC GGAGTGCCTGTGTGGAGGAGACAGCTCCTGTCCGGCATTGTGCAACAGCAAAATAACCTCCTGAGGGCTATCGAAG CCCAACAGCATCTGCTCCAGCTCACCGTCTGGGTCAGGCATTTCCCCAGGCCTTGGCTCCACAGCCTGGGACAGTA CATCTATGAGACATACGGAGACACATGGTCGGGAGTGGAAGCCCTCAAAGCCCTCATCAAACCCAAAAAGATTAAG CCTCCCCTCCCATCCGTGAAAAAGCTCACCGAAGACAAATGGAATAAGCCTCAAAAGACATATAGCGCTGGCGAAA GGATTGTCGATATCATTGCAACCGACATTCAGACTAAGGAACTGCAAAACCAAATCATAAAGATTCAGAATTTCGC TGTGTTTATCCATAACTTTAAGAGGAAGGGAGGCATTGGCGGCTACTCCGCCGGAGAGAATCATTGACATTATC GCCAGCGATATCGTTCCCGTGGGCGATATCTATAAGAGATGGATCATTCTGGGACTCAACAAAATCGTGAGAATGT ATTCACCCGTCAGCATTCTGGATATCAGAGTGAGACAGGGATACTCCCCCCTCAGCTTTCAGACACTGATGCCCGC CCTCTGTCTCAGACAAGGGGAGACAATCCCACAGACCCTAAGGAAAGCAAAAAGGCTAGTGGAGTGGTCGAGTCCA TGAATAAGGAACTGAAAAAGATTATCGGACAGGTCAGGGACCAGGCTGAGCACCTGAAAAACCGCTGTGCAAATGGC CCCATTGCCCCTCTCACCGAGATTTGTAAAGAAATGGAAAAAGAAGGCAAAATCTCCAGGATTGGCCCTGAGAATC CCTATAACACACCCGTCTTTGCCATTCAAGTGAGAGACCAAGCCGAACACCTCAAGACAGCCGTCCAGATGGCAGT GACTTTAGGGAGCTCAACAACGTACACAGGATTTCTGGGAGGTCCAGCTCGGCTTTTCGGCTCTGGCTTGGGATG ACCTCAGGAGCCTGTGTCTGTTCAGCTATCACAGACTGAGAGACTTTATCCTCATCGTTGCCAGAACCTGCCGACA TAGCAGAATCGCCATCACTAGGCAACGTAGAGGTAGGAACGGCTCCTCCAGGTCCGCTGCCCCCAAAATCTCCTTC GACCCCATTCCCATTCACTATTGCGCTCCCGCTGGCTTCGCTATCCTCAAGTGTAACAATAAGACATTCAATGGCG CCTCGCCGATCAGCCTAGCCTCTATCCTCCCTTAGCTTCCCTGAAAAGCCTCTTCGGAAACGATCCCTCATCCCAA GCCGCTAGAAGGGCTATCCTCGGCCAAATAGTCAGGAGAAGGTGTGAGTATCAGTCCGGACACAATAAGGTCGGCT CCCTGCAATACCTTGCACTCAGCCAACCCAAAACCGCTTGCTACAAGTGTTACTGTAAGAAATGTTGCTACCACTG TCAGGTCTGCTTCCTGAAGAAGGGACTGGGAATCAGGGATTACGGAAAGCAAATCGCTGGCGCTGACTGTGTGGCC AGCAGGCAAGACGAAGCCAAGCCAAGTACCATAGCAATTGGAGAACCATGGCCAGTGAGTTTAACCTCCCCCTA TCGTCGCTAAGGAAATCGTCGCAAGTTGTGATAAGTGTAACGAATGGACACTGGAACTGCTGGAGGAACTGAAACA TGAAGCCGTGAGACACTTTCCCAGACCCTGGCTGCATGGCCTCGGTCAACACGATATCATTAGCCTCTGGGATCAG



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TCCCTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTGCTGAAGAGCT ACTCCACCCAAGTGGACCCCGATCTGGCTGACCATCTGATTCACCTCCACTATTTCGATTGCTTTTCCGATAGCGC AATCCATCCCATGGGCCTACACGGAATGGAGGATGAGGAAAGGGAAGTGCTGAAATGGAAATTCGATAGCCATCTG GCAGTCCAGGCCTGAGCCTACCGCACCCCAGCCGAGAACTTTAGATTCGGCATTAGCAAAAAGGCTAAGGGATGG TTTTACAGACACCATTACGAAAGCCAACACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCAGCATGATGACCG CTTGCCAAGGCGTCGGCGGACCCAGTCACAAAGCCAGGGTACTGGCAGAGGCTATGTCCCAGGTGAACAACGCTAA CATTCCTCCCATTGTGCCCAAAGAGATTGTGGCAAACTGTGACAAATGCCAGCTCAAGGGTGAGGCTATGCACGGA CAGGTGGACTGTAGCCCTTCCGAGGGATCAAGACAGGCTAGGAAGAACAGACGTAGAAGGTGGCGTGAGAGGCCAAA GGCAAATCCGCGCCATCTCCGAGTGGATTCTGGGACAGATAAGGGAACCCAGAGGCTCCGACATTGCCGGTACCAC AAGCACACTGCAAGAGCAAATCGCATGGATGACAAACAATCCCCCTGGCATTAAGCAAGAGTTTTGGCATTCCCTAT AACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTCAAGAAAATCATTGGCAGACAGGAGATCCTCG ATCTCTGGGTCTACAATACCCAAGGCTTTTTCCCTGACTGGCAGAATTACACACCCGGACCCGGAATCAGATACCC TAGCAGAGCAAGACAGACAGATTCATGCTATTAGCGAAAGGATTCTCAGCAACTTCCTCGGCAGACCCGCTGAG CCTGTGCCTCTGCAACTGTATAAGACACTGAGAGCCGAACAGGCTACCCAAGAGGTCAAGAATTGGATGACCGACA CACTGCTCGTGCAAAACGCAAACCCTGACTGTGAGAAAGTGTATCTGGCTTGGGTCCCCGCTCATAAAGGCATTGG CGGAAACGAACAGGTGGACAAACTGGTCAGCGCTGGCATTAGGAAAACAGACCCTAACCCTCAGGAAATCGATCTG TGAAATGCAATAACAAAAAGTTCAACGGAACTGGACCCTGTAAGAATGTGTCCACCGTCCAGTGTACCCATGGCCT AGAGCTCAAGAATAGCGCTGTCTCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGAGTGGACCGATAGGGTTATC GAAGTGGTTCAGTCCCAGCATCCCAAAGTGTCCAGCGAAGTGCATATCCCTCTGGGAGACGCTAGGCTCGTCATTA AGACATACTGGGGCCTCCACACAGGCGCTGCTATGGGCGGTAAATGGTCCAAGTGCTCCCTCGTCGGATGGCCCGC AGTGAGAGAGAGAATCAGACAGACACCCCCTGCCGCTGAGGGAGTGCTCAAGACCGGCAAGTACTCCAGGATGAGG AGTGCCCATACCAATGACGTCAAGCAACTGACAGAGGTTGTGCAAAAGATTGCCACAGAGTCTAGCTGGGAGGGTC TGAAATACTTGTGGAATCTGCTCCTGTACTGGGGCCTGGAACTGAAAAACTCCGCCGTCAGCCTCCTGAATGCCAC AGCCATTGTGCTGCCTGAGAAAGAAGGCTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCA TCCCAGATTTACGCCGGAAGAGCCATTGAGGCTCAGCAACACTTGCTGCAACTGACAGTGTGGGGCATTAAGCAAC TGCAAGCCAGAGTGCTCGCCATTGAGAGATACCTCGCCCTCCAGGATAGCGGATCGGAAGTGAATATCGTCACCGA TAGCCAATACGCTCTAGGCATCATTCAGGCTCAGCCTGACAAAAGCGAAAGGGAAATCTCCAACTATACCAATCAG ΑΤΥΤΑΙΌΝΑ ΓΑ ΤΟ ΤΟ ΤΟ ΤΟ ΤΟ ΤΑΓΑΚΟΝΑ ΤΟ ΑΙΘΑΚΟΝΑ ΚΑΙΝΤΑ ΑΙΘΟΝΑ ΤΑ ΑΙΘΟΝΑ ΤΟ ΤΟ ΑΙΘΑΚΟΝΑ ΤΑ ΑΙΘΑΚΟΝΑ ΤΑ ΑΙΘΑΚΟΝΑ ΤΑ Α AGAGAAGGGTCGTGCAAAGGGAAAAGCGTGCCGTCGGCATTGGCGCTATGTTTTTCGGATTCCTCGGCGCTGCCAA ACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGACCAAATCCTTATCGAAATCTGTGGA CAGAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGTCGCTAGGATTGTGGAACTGCTCGGCCATA GCTCCCTGAGAGGCCTCCGGAGAGGCACACTGAATGCCTGGGTGAAAGTGGTTGAGGAAAAGGGATTCAATCCCGA AGTGATTCCCATGTTTACCGCTCTGTCCGAGGGAGCCACACTCGAGtgaagatctgaattc

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#### C1 fragment

ggatccaccATGCTCGAGAGCAACACCCCGCTAATAATGCCGATTGCGCGTGGCTGAAAGCCCAGGAAGAGAAG AAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCTTGGAGGGCTATCCTCAACATTCCCAGGAGGATTAGGCA AGGCTTTGAGAGAGCCCTCCTAGCCGCCGAATGGGACAGGGTTCACCCTGTGCACGCTGGCCCTGTCGCTCCCGGC CAAATGAGAGGCCCAGAGGAAGCGATATCGCTGGCACAACCCTCAGGCCCATGACATATAAGGCCGCTATTGACC TCAGCTTGTTTCTGAAAGAGAAAGGCGGACTGGAAGGCCTCATCTATAGCAAGAAAGCTGCTATGGAACAGGCTCC CAAGGCCAATGGACCTACCAAATCTTTCAGGAACCCTTTAAGAATCTGAAAACCGGAAAGTATTCCAGAATGAGAA GCGCTCACACAAACTGGATGACAGAAACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGTCCATCCTCAGGGC TCTGGGAACCGGAGCCACACTGGAAGAGCCTGAGGTCATCCCTATGTTCTCAGCCCTCAGCGAAGGCGCTACCCCC CAAGACCTGAATACGATGCTCAACATCGTCAGCGGACACCAATCCACCCTCCAGGAACAGATTGGCTGGATGACAA ATAACCCTCCCATCCTGTCGGAGAGATTTACAAAAGGTGGATTATCCTCGGCCTGACTAGAATCCCCCATCCCGC CGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACGAAGAC CAAAAGGAAACCTGGGAGGCTTGGTGGACGGAATACTGGCAGGCTACCTGGATTCCTGAGTGGGAGTTTGTGAATA CCCCTCCCTCGTGTTTCCCGATTGGCATAACTATACCCCTGGCCCTGGCATAAGGTATCCCCTCACCTTTGGATG GTGCTTTAAGCTCGTGCCTGTGGACCCCAAACTGTGGTACCAACTGGAAAAGGAACCCATTGTCGGAGCCGAAACC TTTTACGTGGACGGAGCCGCCAACAGAGAGACAAAGCTCGGCCAAAACGTCCAGGGACAGATGGTGCATCAGGCTA TTAGCCCCAGGACCCTCAACGCTTGGGTCAAGGTCGTCGAAGAGAAAGCCTTTAACGAAACCGAAGTGCATAACGT CTGGGCTACCCATGCCTGTGTGCGTACCGATCCCAATCCCCAAGAGATTCTCCTGGAGAATGTGACAGAGCTCAAG GATCAGAAACTCCTCGGCATTTGGGGATGCTCCGGCAAAATCATTTGCACAACCACTGTGCCTTGGAACAGCTCCT GGTCCAACCAAGCTGGCCATAACAAAGTGGGAAGCCTCCAGTATCTGGCTCTGACGGCTCTGATTAAGCCTAAGAA AATCAAACCCCCTCTGCCTAGCGTTAAGACAATCATTGTGCATCTGAATGAGTCCGTGGAAATCAATTGCACAAGG CCTAACAATAACACAAGGAAAGCCGCCGCTAGTGAAGTACGGAATAAGTCCAAACAGAAAACCCAGCAAGCTGCCG CCGATACAGGCGACTCCAGCCAGGTCAGCCAAAACTATCCCATTGTGTCCAACTTTACCTCCACCACTGTGAAAGC CGCTTGTTGGTGGGCCAATATCAAACAGGAGTTTGGAATCCCTTACAATCCCCAAAGCCCAAACATTCTATGTGGAT GAATCTGGCAGCTCGACTGTACCCATCTGGAAGGCAAAGTCATTCTGGTAGCCGTCCACGTCGCCTCCGGCTACAT TGAGGCTGAGGTCGGCAATGAGCAAGTGGATAAGCTCGTGAGTTCCGGAATCAGAAAGGTGCTATTCCTCGACGGA ATCAATAAGGCTCAGGAAGAGCACGAAGTCAGGGAAAGGATTAGGCGAACCGCTCCCGCTGCTGAAGGCGTCGGCG CTGTCTCCCAGGATCTGGATAAGTACGGAGCCCTCACCTCCACAAGCGGAACCCAACAGTCCCAGGGAACTGAAAC TGGCGTCGGCAACCCTCAGATTTTGGGAGAGTCCAGCGTTGTCCTCGGCTCCGGCTCCATCGTCATCTGGGGTAAA ACCCCTAAGTTTAAGTTCCCCATTCAGAAAGAGACATGGGAAGCCTGGTGGACGAGTATTGGCAAGCCGCTGCTT ACAGACTGATCAGCTGTAACACAAGCGTTATCAAACAGGCTTGCCCTAAGATTACCTTTGACCCTATCCCTATCCA TTACTGTGCCCCTCCTAGCTGGATGGGCTATGAGCTCCACCCTGACAGATGGACAGTGCAACCCATCGTGCTCCCC GAAAAGGACTCCTGGACAGTGAATGACATTCAGAAATCAATTCTGAGAGCCCTCGGCCCAGGCGCTTCCCTGGAGG AAATGATGACAGCATGTCAGGGAGTGGGAGGCCCTGGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCC CATTTGGAAAGGCCCTGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGC CAACTGATAGAAGCCCTCCTGGATACAGGAGCCGATGACACCGTCCTGGAAGATATGAATCTGCCTGGCAAGTGGG GAATCAAACAGCTCCAGGCTAGGGTCCTGGCTATCGAGAGGTATCTGAAAGATCAACAGTTTCTGGGACTCTGGGG CTGTAGCGGAAAGGCTGCTATGGAAAACAGATGGCAAGTGATGATCGTCTGGCAAGTGGACAGGATGAAGATTAGG

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ACATGGAATAGCCTCGTGAAACACCATATGTATATTATCTGTACCACAACCGTCCCCTGGAACTCCACCTGGAGCA ATAAGTCCTTCGAAGAGATTTGGAATAACATGACCTGGATTCAATGGCTGATTCTCGCTATCGTCGTGTGGACCAT TGTGTATATCGAATACAAGAAACTGCTCAGGCAAAGGAGAATCGATAGGCTCATCAAAAGGCTCAACCCTGGCCTC CAATGAGTCCGAGGGAGACACCCCGGAATCAGATACCAATACAATGTGCTCCCCCAAGGCTGGAAGGGCTCCCCA CCCATTTTCCAAAGCTCCATGACCCAAATCCTCATGATGCAAAGGGGAAACTTTAAGGGACAGAAAAGGATTATCA AGTGCTTCAACTGTGGAAAGGAAGGCCATCTCGCTAGGAATTGCAGACCTCCCCTAGAGAGACTGAACCTGGATTG CTCCGAGGATAGCGACACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGAAGTGGGACTCGTGGCTGTGCAT GTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTATCCTCAAGA TTAAGCCTGTGGTCAGCACACAGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGAAATCATTATCAGAAGCGAAAA CTTTACCGATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACGCTGGCATCAAAGTGAAGCAACTG ATGTGAATGCTGCTCAAACCAGAGGCGATAACCCTACCGGTCCCGAAGAGTCCAAGAAGAGGTCGCGTCCAAGAC AGAGACAGACCCTTGTGACGCCGCCCCTAGCTCCAACTTTCTGGGAAGGTCTGCCGAACCCGTCCCCCTCCAGCCC CCCCTCTGGAAAGGCTCCACCTCGACTGTAGCGAAGACTGTGGCGAACTGGATAAGTGGGCCTCCCTGTGGAACT GGTTCAATATCACCAACTGGCTGTGGTACATTAAGATTTTCATTATGATTGTGGGAGGCAATAAGATTGTCAGGAT GTACTCACCTGTCTCCATCCTCGACATTAAGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTCGCT AAGCTCCTGTGGAAGGGAGGGGGGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGG CTAAGATTATCGAACTGAATAAGAGAACCCAAGACTTTTGTGAAGTGCAACTGGGAATCCCTCACCCTGCTGGACT GAAGAAGAAAAGTCAGTGACAGTGGCCGCTATGAGAGTGAAAGAGACACAGATGAACTGGCCCAATCTGTGGAAG TGGGGCACAATGATTCTGGGACTGGTCATCATTTGCTCCGCCTCCATTAAGGTCAGACAGCTCTGCAAACTGCTCA GGGGTACAAAGGCTCTGACAGAGATTGTGACACTGACAGAGGAAGCCGAACTGGAACTGCTCATATGGAAGTTTGA CTCCCGCCTCGCCTGAGACATATCGCCAGGGAACTGCATCCCGAGTTCTACAAAGACTGCGCTGCTGTCGAGCTC GGGGCTCTAGCCTGGGGCAACTGCAACCTGCTCTGAAAACCGGATCAGAGGAACTGAAGTCCCTGTATAACACAAT CGCTACCCTCTGGTGTGCATCAGGAGCTCTACAAATACAAAGTGGTCAAAATCAAACCCCTCGGCATTGCCCCT ACCAGAGCCAAAAGGAGAGTGGTCGAGAGAGAGAAAAGGCTCACCGAAATCGTCCCACTCACCGAAGAGGCTGAGC TGGAGCTGGAGGAAAACAGAGAGATTCTGAGGGAACCCGTCCACGGAGTGTATAGAGTGCTCGCCGAAGCCATGAG CCAAGTCAACAATGCCAACATCATGATGCAGAGAGGCAATTTCAAAGGCCTAAAGAGAATCATCAAACAAGAGGAA GAGGAGGTCGGCTTCCCCGTCAGGCCCCAGGTCCCACTGAGACCTATGACCTACAAAGGAGCCGTCGATCTGTCCT TCTTCAGACAGGGACCCAAAGAGCCTTTCAGAGACTATGTGGATAGGTTTTTCAAAACCCTCAGGGCTGAGCAAGC CTCACAGGAAGTGAAAAACTGGGAGAAAATCAGACTGAGACCTGGTGGCAAAAAGAAATACAAAATGAAACACATT GTGTGGGCCTCCAGGGAACTGGAAAGGTTTGCCTCCCAGTATGCCCTCGGCATCATCCTAGCCCAACCCGATAAGT GGGCTGATGTGAAACAGCTCACCGCAGTCGTCCAGAAAATCGCTACCGAAAGCATTGTGATATGGGGAAAGACGCC CAAGTTCAGACTGCCTATCGCTGCCGCCAGCAACGAGAACATGGAGACCATGGCTGCTtgaagatctgaattc

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#### C2 fragment

qqatccaccATGCTCGAGAGCAACACAGCCGCTAACAATACCGATTGCGTGTGGCTGAAAGCCCAGGAAGAGAGAAG **AAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCCGGGAGGGCTATCCTCAACATTCCCACGAGGATTAGGCA** AGGCCTTGAGAGAGCCCTCCTAGCCGCCGAATGGGATAGGATTCACCCTGTGCACGCTGGCCCTATCGCTCCCGGC CAAATGAGAGAGCCCAGGGGAAGCGATATCGCTGGCACAACCCTCAGGCCCATGACATATAAGGCCGCTATTGACC TCAGCTTGTTTCTGAAAGAGAAAGGCGGACTGGATGGCCTCATCTATAGCAAGAAAGCTGCTATGGAACAGGCTCC CGAAGACCAAAGCTCTCAGAGAGAGCCTTACAATGAGTGGACCCTGGAGCTCCTGGAAGAGCTCAAGCACGAGGCT CAAGGCCAATGGACCTTCCAAATCTTTCAGGAACCCTTTAAGAATCTGAAAACCGGAAAGTATGCCAGAATGAGAG GCGCTCACACAAACTGGATGACAGATACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGTCCATCCTCAAGGC TCTGGGACCCGGAGCCTCACTGGAAGAGCCTGAGGTCATCCCTATGTTCTCAGCCCTCAGCGAAGGCGCTACCCCC CAAGACCTGAATATGATGCTCAACACCGTCGGCGGACACCAATCCACCCTCCAGGAACAGATTGGCTGGATGACAA ATAACCCTCCCATCCCTGTCGGAGAGATTTACAAAAGGTGGATTATCCTCGGCCTGACTAGAATCCCCCATCCCGC CGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACGAAGGC CAAAGGGAAACCTGGGAGGCTTGGTGGATGGAATACTGGCAGGCTACCTGGATTCCTGAGGGGGAGTTTGTGAATA CCCCTCCCTCGTGTTTCCCGATTGGCAAAACTATACCCCTGGCCCTGGCACAAGGTATCCCCTCACCTTTGGATG GTGCTTTAAGCTCGTGCCTGTGGACCCCAAACTGTGGTACCAACTGGAAAAGGACCCCATTGTCGGAGTCGAAACC TTTTACGCGGACGGAGCCGCCAACAGAGAGACAAAGCTCGGCCAAAACGTCCAGGGACAGATGGTGCATCAGCCTA TTAGCCCCAGGACCCTCAACGCTTGGGTCAAGGTCATCGAAGAGAAAGGCTTTAGCGACACCGAAGTGCATAACGT CTGGGCTACCCATGCCTGTGTGCCTACCGATCCCAATCCCCAAGAGATTCTCCTGGAGAATGTGACAGAGCTCAAG GATCAGAAACTCCTCGGCATTTGGGGATGCTCCGGCAAACTCATTTGCACAACCACTGTGCCTTGGAACAGCTCCT GGTCCAACCCAGCTGGCCATAACAAGTGGGAAGCCTCCAGTATCTGGCTCTGAAGGCTCTGATTACGCCTAAGAA AATCAAACCCCCTCTGCCTAGCGTTAAGACAATCATTGTGCATCTGAATGAGTCCGTGGAAATCAATTGCACAAGG CCGATACAGGCAGCTCCAGCAAGGTCAGCCAAAACTATCCCATTGTGTCCAACTTTACCTCCACCACTGTGAAAGC CGCTTGTTGGTGGGCCAATATCAAACAGGAGTTTGGAATCCCTTACAATCCCCAAAGCCGAACATTCTATGTGGAT GAATCTGGCAGCTCGACTGTACCCATCTGAAAGGCAAAGTCATTCTGGTAGCCGTCCACGTCGCCTCCGGCTACAT TGAGGCTGAGGTCGGCAATGAGCAAGTGGATAAGCTCGTGATTTCCGGAATCAGAAAGGTGCTATTCCTCGACGGA ATCGATAAGGCTCAGGAAGAGCACGAAGTCAGGGAAAGGATTAGGCGAGCCGCTCCCGCTGCTGAAGGCGTCGGCG CTGTCTCCCAGGATCTGGATAAGTACGGAGCCATCACCTCCACAAGCGGAACCCAACAGTCCCAGGGAACTGAAAC TGGCGTCGGCAACCCTCAGATTTTGGGAGAGTCCAGCGCTGTCCTCGGCTCCGGCTCCATCGTCATCTGGGGTAAA ACAGACTGATCAGCTGTAACACAAGCGTTATCACACAGGCTTGCCCTAAGATTAGCTTTGAGCCTATCCCTATCCA TTACTGTGCCCCTCCTAGCTGGATGGGCTATGAGCTCCACCCTGACAGATGGACAGTGCAACCCATCGTGCTCCCC GAAAAGGAGTCCTGGACAGTGAATGACATTCAGAAAACAATTCTGAAAGCCCTCGGCCCAGGCGCTACCCTGGAGG **AAAATATGACAGCATGTCAGGGAGTGGGAGGCCCTGGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCC** CATTTGGAAAGGCCCTGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGC CAACTGAAAGAAGCCCTCCTGGATACAGGAGCCGATGACACCGTCCTGGAAGATATCAATCTGCCTGGCAAGTGGG GAATCAAACAGCTCCAGGCTAGGGTCCTGGCTATCGAGAGGTATCTGAAAGATCAACAGCTTCTGGGAATCTGGAG CTGTAGCGGAAAGGCTGCTATGGAAAACAGATGGCAAGTGATGATCGTCTGGCAAGTGGACAGGATGAAGATTAGG

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ACATGGAATAGCCTCGTGAAACACCATATGTATCTTATCTGTACCACGCCGTCCCCTGGAACTCCACCTGGAGCA ATAAGTCCTTCGAAGAGATTTGGAATAACATGACCTGGATTGAATGGCTGATTATCGCTATCGTCGTGTGGACCAT TGTGTTTATCGAATACAAGAAACTGCTCAGGCAAAGGAAAATCGATAGGCTCATCGAAAGGCTCAACCCTGGCCTC CAATGAGTCCGAGGGAGACACCCCGGAATCAGATACCAATACAATGTGCTCCCCAAGGCTGGAAGGGCTCCCCA GCCATTTTCCAAAGCTCCATGACCAAAATCCTCATGATGCAAAGGGGGAAACTTTAAGGGACAGAAAAGGATTATCA AGTGCTTCAACTGTGGAAAGGAAGGCCATCTCGCTAGGAATTGCAGACCTCCCCTGGAGAGACCTGAACCTGGATTG CTCCGAGGATAGCGACACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGGAGTGGGACTCGTGGCTGTGCAT GTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTCTCCTCAAGA TTAAGCCTGTGGTCAGCACACACTCCTGCTCAACGGTAGCCTCGCTGAAGAGAGAAATCATTATCAGAAGCGAAAA CTTTACCAATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACCCTGGCATCAAAGTGAGGCAACTG AGAGACAGACCCTTTTGACGCCGCCCCTAGCTCCACCTTTCTGGGAAGGTCTGTCGAACCCGTCCCCCTCCAGCTC GGTTCAATATCACCAACTGGCTGTGGTACATTAAGATTTTCATTATGATTGTGGGAGGCAATAAGATTGTCAGGAT GTACCAACCTGTCTCCATCCTCGACATTAAGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTCGCT AAGCTCCTGTGGAAGGGAGGGAGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGG CTAAGATTATCGAACTGAATAAGAGAACCCAAGACTTTTGGGAAGCGCAACTGGGAATCCCTCACCATGCTGGACT GAAAAAGAAAAAGTCCGTGACAGTGGCCGCTATGAGAGTGAAAGAGACACAGATGAACTGGCCCAATCTGTGGAAG TGGGGCACAATGATTCTGGGACTGGTCATCATTTGCTCCGCCTCCATTAAGGTCAAACAGCTCTGCAAACTGCTCA GGGGTGCAAAGGCTCTGATAGACATTGTGCCACTGACAGAGGAAGCCGAACTGGAACTGCTCATATGGAAGTTTGA  $\tt CTCCCACCTCGCCTGAGACATATCGCCAGGGAACTGCATCCCGAGTACTACAAAGACTGCGCTGCTGTCGAGCTC$  $\tt CTGGGACGCTCCAGCCTCAAGGAACTGCGAAGGGGATGGGAAGCCCTCAAGTATTTGTGGAACCTCCTGCAGTATT$ GGGGCTCTAGCCTGGAGCAACTGCAATCTGCTCTGAAAACCGGATCAGAGGAACTGAGGTCCCTGTTTAACACAGT CGCTACCCTCTGGTGTGTGCATCAGGAGCTCTACAAATACAAAGTGGTCAAAATCGAACCCCTCGGCATTGCCCCT ACCAAAGCCAAAAGGAGAGTGGTCCAGAGAGAGAAAAGGCTCACCGATATCGTCACACTCACCGAAGAGGCTGAGC TGGAGCTGGAGGAAAACAGAGAGATTCTGAAGGAACCCGTCCACGGAGTGTATAGAGTGCTCGCCGAAGCCATGAG CCAAGCCAACAATGCCAACATCATGATGCAGAGAGGCCAATTTCAGAGGCCCAAAGAGAATCATCAAACAAGAGAAA GAGGGGGTCGGCTTCCCCGTCAGGCCTCAGGTCCCACTGAGACCTATGACCTACAAAGCAGCCATCGATCTGTCCT TCTTCAAACAGGGACCCAAAGAGCCTTTCAGAGACTATGTGGATAGGTTTTTCAAAACCCTCAGGGCTGAGCAAGC CTCACAGGAAGTGAAAAACTGGGAGAAAATCAGACTGAGATCTGGTGGCAAAAAGAAATACAAACTGAAACACATT GTGTGGGCCTCCAGGGAACTGGAAAGGTTTGCCTCCCAGTATGCCCTCGGCATCATCCTAGCCCAACCCGATAAGT GGGCTGATGTGAAACAGCTCACCGAAGTCGTTCAGAAAATCGCTACCGAAAGCATTGTGATATGGGGAAAGACACC CAAGTTCAGACAGCCTATCGCTGCCGCCAGCAACGAGAACATGGACGCCATGGCTGCTtgaagatctgaattc

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## INTERNATIONAL SEARCH REPORT

Internati pplication No PCT/ 03/00698

A. CLASSIFICATION OF SUBJECT MATTER 1PC 7 C07K14/47 A61K38/17 C07K19/00 C12N15/62

C12N15/12

C12N5/08

C12P37/04

Relevant to claim No.

1,2,4-9

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Category °

Χ

Minimum documentation searched (classification system followed by classification symbols)

A61K C12P C07K C12N IPC 7

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, MEDLINE, CHEM ABS Data, WPI Data

Citation of document, with indication, where appropriate, of the relevant passages

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X Further documents are listed in the continuation of box C.	X Patent family members are listed in	n annex.
Special categories of cited documents:  "A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the inte or priority date and not in conflict with cited to understand the principle or th invention	rnational filing date the application but eory underlying the
<ul> <li>"E" earlier document but published on or after the international filing date</li> <li>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</li> <li>"O" document referring to an oral disclosure, use, exhibition or other means.</li> <li>"P" document published prior to the international filing date but later than the priority date claimed</li> </ul>	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  "8" document member of the same patent family	
Date of the actual completion of the international search	Date of mailing of the international sea	rch report
19 December 2003	1 0. 05. 2004	
Name and mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  Fax: (+31-70) 340-3016	Authorized officer  Groenendijk, M	
Form PCT/ISA/210 (second sheet) (January 2004)		

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## INTERNATIONAL SEARCH REPORT

International Application No PCT, 93/00698

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT	1017 03700030
Category ° Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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ROMERO P ET AL: "Therapeutic cancer vaccines based on molecularly defined human tumor antigens" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 20, 19 December 2002 (2002-12-19), pages A2-A7, XP004397465 ISSN: 0264-410X the whole document	1,2,8
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BENLALAM H ET AL: "Comprehensive analysis of the frequency of recognition of melanoma-associated antigen (MAA) by CD8 melanoma infiltrating lymphocytes (TIL): implications for immunotherapy."  EUROPEAN JOURNAL OF IMMUNOLOGY. GERMANY JUL 2001, vol. 31, no. 7, July 2001 (2001-07), pages 2007-2015, XP002265727 ISSN: 0014-2980 cited in the application figure 1	

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The International Searching Authority has determined that this international application contains multiple (groups of) inventions, as follows:

1. Claims: 1-10 (in part)

Use of at least one peptide comprising the EX1AGIGILX2 sequence as defined in claim 1a; peptides of sequences 9-12, their compositions defined in claims 4-6, polynucleotides coding the same, presenting cells containing the same as defined in claims 8 and 9, and their diagnostic use.

2. Claims: 1-10 (in part)

Use of at least one peptide comprising the EVDPIGHVY sequence as defined in claim 1b; their compositions defined in claims 4-6, polynucleotides coding the same, presenting cells containing the same as defined in claims 8 and 9, and their diagnostic use.

3. Claims: 1-10 (in part)

Use of at least one peptide comprising the VPLDVCLYR sequence as defined in claim 1c; peptides of sequences 3, 13 and 14, their compositions defined in claims 4-6, polynucleotides coding the same, presenting cells containing the same as defined in claims 8 and 9, and their diagnostic use.

4. Claims: 1-10 (in part)

Use of at least one peptide comprising the TPRLPSSADVEF sequence as defined in claim 1d; peptides of sequences 4 and 15, their compositions defined in claims 4-6, polynucleotides coding the same, presenting cells containing the same as defined in claims 8 and 9, and their diagnostic use.

5. Claims: 1-10 (in part)

Use of at least one peptide comprising the MPFATPMEA sequence as defined in claim 1e; their compositions defined in claims 4-6, polynucleotides coding the same, presenting cells containing the same as defined in claims 8 and 9, and their diagnostic use.

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patent family members

Information

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International Application No

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